COMPARISON OF PERINEURAL AND INTRAVENOUS DEXAMETHASONE ON DURATION OF ANALGESIA IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

Dissertation Submitted to

The Tamil Nadu Dr.M.G.R Medical University for MD Degree examination in Anesthesiology to be held in

May 2018

DEPARTMENT OF ANESTHESIOLOGY

PSG INSTITUTE OF MEDICAL SCIENCES

& RESEARCH, COIMBATORE

CERTIFICATE

This is to certify that this dissertation entitled **"COMPARISON OF PERINEURAL AND INTRAVENOUS DEXAMETHASONE ON DURATION OF ANALGESIA IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK**" done by Dr.J.KEERTHANA, post graduate student (2015-2018) in the Department of Anesthesiology, PSG Institute of Medical Sciences & Research, Coimbatore, under the direct guidance and supervision of guide Prof. Dr. S. SHAIK MUSHAHIDA in partial fulfillment of the regulations laid down by the Tamil Nadu Dr.M.G.R. Medical University, Chennai for MD Anesthesiology degree examination.

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DECLARATION

I, Dr.J.KEERTHANA, hereby declare that this dissertation entitled **“COMPARISON OF PERINEURAL AND INTRAVENOUS DEXAMETHASONE ON DURATION OF ANALGESIA IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK** " done by me is being submitted in partial fulfillment for the award of M.D. degree in Anesthesiology by the Tamil Nadu MGR Medical University in the examination to be held in May 2018.

Place : Coimbatore **Dr. J.KEERTHANA**

Date :

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Institutional Human Ethics Committee

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To
Dr J Keerthana
Postgraduate
Department of Anaesthesiology
Guide: Dr S Mushahida
PSG IMS & R
Coimbatore

Ref: Project No.15/384

Date: December 30, 2015,

Dear Dr Keerthana,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 17.12.2015 to conduct the research study entitled *"Comparison of perineural and intravenous dexamethasone on duration of analgesia in supraclavicular brachial plexus block"* during the IHEC review meeting held on 28.12.2015.

The following documents were reviewed and approved:

1. Project Submission form
2. Study protocol (Version 1 dated 17.12.2015)
3. Informed consent forms (Version 1 dated 17.12.2015)
4. Data collection tool (Version 1 dated 17.12.2015)
5. Current CVs of Principal investigator, Co-investigator
6. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 28.12.2015 at Research Conference Room, PSG IMS & R between 10.00 am and 12.30 pm:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mrs Y Ashraf	MPT	Physiotherapy	Female	Yes	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Mr Gowpathy Velappan	BA., BL	Legal Advisor	Male	No	No
4	Dr A Jayavardhana	MD	Clinician (Paediatrics)	Male	Yes	Yes
5	Mr P Karuppuchamy	M Phil in PSW	Social Scientist	Male	Yes	Yes
6	Mrs G Malarvizhi	M Sc	Nursing	Female	Yes	Yes
7	Mr. R. Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
8	Dr. Parag K Shah	DNB	Clinician (Ophthalmology)	Male	No	No

9	Dr. G. Rajendiran	DM	Clinician (Cardiology)	Male	Yes	Yes
10	Mrs P Rama	M Pharm	Non-Medical (Pharmacy)	Female	Yes	Yes
11	Dr. Seetha Panicker (Vice-chairperson, IHEC)	MD	Clinician (Obstetrics & Gynaecology)	Female	Yes	Yes
12	Dr R Senthil Kumar	MD	Clinician (Endocrinology)	Male	Yes	Yes
13	Dr. S. Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
14	Dr. Sudha Ramalingam (Alternate Member-Secretary, IHEC)	MD	Public Health, Epidemiology, Genetics, Ethicist	Female	Yes	Yes
15	Mrs. Swasthika Soundararaj	MBA	Lay person	Female	No	Yes
16	Dr. D. Vijaya	M Sc, Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
6. In the event of any protocol amendments, IHEC must be informed and the amendments should be highlighted in clear terms as follows:
    a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
    b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
    c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
    d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
    e. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented

f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review

7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Thanking You,

Yours Sincerely,

SECRETARY
PSG IMS&R
COIMBATORE-641004.

Dr S Bhuvaneshwari
Member - Secretary
Institutional Human Ethics Committee

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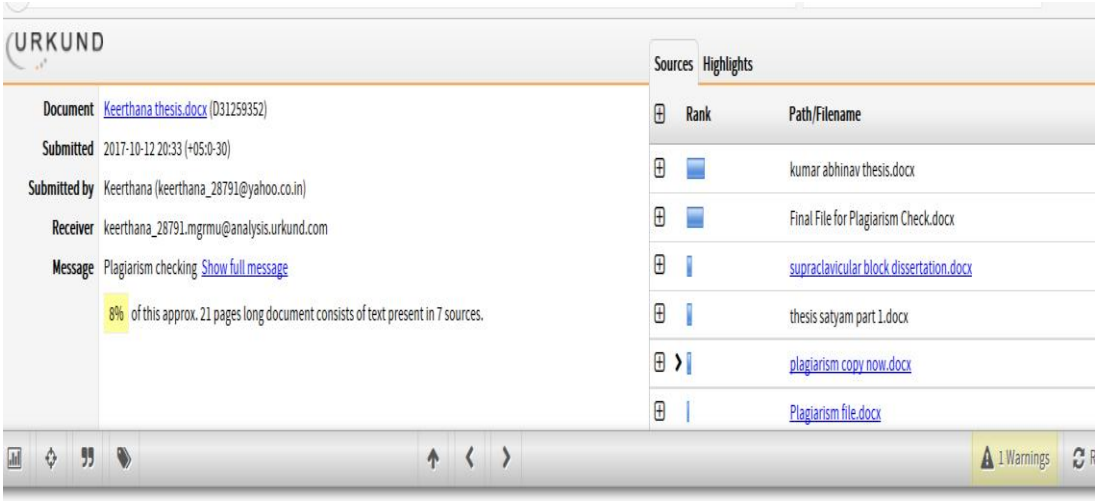

INTRODUCTION

Pain is the most common complaint by the patients in the post-operative period and pain management is one of the important components in peri-operative care1. Supplementation of excessive opioids and other analgesics such as Non steroidal anti-inflammatory drugs (NSAID'S) for pain management often become necessary in most of the cases. Opioids have their own side effects such as nausea, vomiting and respiratory depression and dependence when used in large doses. NSAID's are contraindicated in patients with renal and liver dysfunction2. In order to minimise the side effects of analgesics, to reduce poly pharmacy and to provide adequate analgesia, additives are added to peripheral nerve blocks to achieve the same3. Brachial plexus nerve blocks with additives for upper limb surgeries provide superior analgesia, avoids side effects of general anaesthesia and also minimises use of analgesics in the post-operative period4,5. Single shot Brachial Plexus block provides analgesia in the immediate post-operative period but often fail to provide extended analgesia as post-operative pain can exist for several days1. Thus measures to prolong the duration of sensory blockade often becomes mandatory in almost all cases. Continuous peripheral nerve block with the use of catheters can be used to provide a period of extended analgesia but is often associated with complications such as catheter migration, leakage of the local anaesthetic and infection,6,7,8. Lack of expertise to perform continuous peripheral nerve blockade and lack of continuous monitoring is also a major problem with continuous nerve block catheters. Various additives have been studied in an attempt to enhance the effect of single shot nerve blockade. Many additives have been used with local anaesthetics to prolong the duration of blockade by producing local vasoconstriction or delaying diffusion of local anaesthetic from the site of injection. Some of the additives used with local anaesthetics include alpha 2 agonists, NSAID'S, opioids, and glucocorticoids9. Addition of long acting glucocorticoids like Methylpredinosolone with local anaesthetics have been used to treat chronic pain10. Addition of Dexamethasone with local anaesthetics in peripheral nerve blocks to prolong duration of analgesia is being extensively studied. Many studies have shown

CERTIFICATE – II

This is to certify that this dissertation work titled **"COMPARISON PERINEURAL AND INTRAVENOUS DEXAMETHASONE ON DURATION OF ANALGESIA IN SUPRACLAVICULAR BRACHIAL PLXUS BLOCK"** of the candidate Dr. J. KEERTHANA with registration Number 201520401 for the award of M.D in the branch of Anesthesiology. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 8% (Eight percentage) percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

ACKNOWLEDGEMENT

First and foremost my salutations to God the almighty for his divine grace bestowed upon me.

With proud privilege and deep sense of respect I express my heartfelt gratitude to my guide **Dr.S.Mushahida** for her suggestions, help, critical reviews and constant motivation rendered through out the preparation of this dissertation.

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Finally I convey my heartfelt gratitude to all my **Patients** without whose co-operation this study would not have been possible.

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INTRODUCTION

Pain is the most common complaint by the patients in the post-operative period and pain management is one of the important components in peri-operative care[1.] Supplementation of excessive opioids and other analgesics such as Non steroidal anti-inflammatory drugs (NSAID'S) for pain management often become necessary in most of the cases. Opioids have their own side effects such as nausea, vomiting and respiratory depression and dependence when used in large doses. NSAID's are contraindicated in patients with renal and liver dysfunction[2]. In order to minimise the side effects of analgesics, to reduce poly pharmacy and to provide adequate analgesia, additives are added to peripheral nerve blocks to achieve the same[3]. Brachial plexus nerve blocks with additives for upper limb surgeries provide superior analgesia, avoids side effects of general anaesthesia and also minimises use of analgesics in the post-operative period[4,5].

Single shot Brachial Plexus block provides analgesia in the immediate post-operative period but often fail to provide extended analgesia as post-operative pain can exist for several days[1]. Thus measures to prolong the duration of sensory blockade often becomes mandatory in almost all cases. Continuous peripheral nerve block with the use of catheters can be used to provide a period of extended analgesia but is often associated with complications such as catheter migration, leakage of the local anaesthetic and infection[,6,7,8]. Lack of expertise to perform continuous peripheral nerve

blockade and lack of continuous monitoring is also a major problem with continuous nerve block catheters.

Various additives have been studied in an attempt to enhance the effect of single shot nerve blockade. Many additives have been used with local anaesthetics to prolong the duration of blockade by producing local vasoconstriction or delaying diffusion of localanaesthetic from the site of injection. Some of the additives used with local anaesthetics include alpha 2 agonists, NSAID'S, opioids, and glucocorticoids[9]. Addition of long acting glucocorticoids like Methylpredinosolone with local anaesthetics have been used to treat chronic pain[10]. Addition of Dexamethasone with local anaesthetics in peripheral nerve blocks to prolong duration of analgesia is being extensively studied.

Many studies have shown that addition of Dexamethasone perineurally does increase the duration of analgesia. There are concerns regarding potential neural toxicity with use of perineural Dexamethasone but the evidences remain inconclusive[11,12]. The use of intravenous Dexamethasone as a safe alternative to perineural Dexamethasone in prolonging the analgesia duration is being studied and investigated recently.

In our study we have compared the analgesic duration between patients receiving Dexamethasone 8 milligram perineurally and by the intravenous (IV) route in supraclavicular brachial plexus block. We have also compared the difference, if any between the onset of sensory and motor blockade in both the groups.

AIM OF THE STUDY

PRIMARY AIM:

The aim of the study is to compare the effects of perineural and IV Dexamethasone in the duration of analgesia in adult patients undergoing elective upper limb surgeries under Supraclavicular Brachial Plexus block.

SECONDARY AIM:

To find out the difference if any between the onset of sensory and motor blockade in patients receiving perineural and IV Dexamethasone.

REVIEW OF LITERATURE

Desmet et al, performed a prospective randomised double blinded study with perineural and intravenous Dexamethasone in 150 patients posted for various shoulder surgeries under interscalene block. The study participants were divided into three groups. The control group received 30ml of 0.5% Ropivacaine only. The perineural group received 30 ml of ropivacaine with Dexamethasone 8mg.The IV group received 30ml of Ropivacaine and Dexamethasone 8mg in the IV route. Block was performed using a nerve stimulator.

Primary outcome was the duration of analgesia which was identified with the verbal analogue scale and the time of first analgesic administration. The median time of sensory block was equivalent in both IV and perineural groups. The opioid consumption in the first 24 hours following surgery was also less in both IV and perineural groups. They concluded that both IV and perineural Dexamethasone are equivalent in prolonging analgesic duration with single shot interscalene block[1].

Rosenfeld et al, compared the effects of IV and perineural Dexamethasone administered concomitantly for interscalene block. The study included 150 patients with 50 in each group. The control group received 28 ml of Ropivacaine with 2 ml of normal saline. The IV group received 28 ml of Ropivacaine with Dexamethasone in the IV route and the other group received Ropivacaine with perineural Dexamethasone There was no significant

difference in the onset of sensory and motor blockade between the two groups as compared to the control group. The mean duration of analgesia was prolonged in IV and perineural groups and the duration was almost similar in both groups[12].

Abdallah et al, did a randomised triple arm double blinded study and compared the duration of analgesia with IV and perineural Dexamethasone after supraclavicular block. In their study seventy five patients were randomised to receive supraclavicular block with 30 ml bupivacaine alone in the control group, 30 ml of Bupivacaine with 8mg Dexamethasone perineurally and 30ml of Bupivacaine with 8mg Dexamethasone intravenously. The superiority of IV Dexamethasone was first compared with the control group and then with the perineural group. Apart from analgesia duration, motor block duration, pain scores, opioid consumption and block related complications were also analysed.

The study participants were divided into twenty five in each group. Duration of analgesia was prolonged in IV group than the control group and was similar to the perineural group. Both IV and perineural groups had reduced pain scores and reduced opioid consumption in the post-operative period as compared with the control group. They concluded that effectiveness of IV Dexamethasone in prolonging duration of analgesia in supraclavicular block is similar to perineural Dexamethasone[13].

Parveen et al, studied the effect of IV dexamethasone in prolonging analgesia in supraclavicular block in 80 patients undergoing elective orthopaedic procedures of the upper limb under supraclavicular brachial plexus block. The study participants were divided into two groups. One group received 30 ml of ropivacaine and 2.5 ml of normal saline intravenously. The other group received 30 ml of ropivacaine with 10 mg dexamethasone in the IV route. The block was performed using a nerve stimulator.

The parameters noted were onset of sensory and motor blockade and duration of sensory blockade. The onset of sensory blockade was tested by pinprick method. Onset of motor blockade was tested by modified Bromage scale. In the post operative period motor blockade and verbal pain rating scores were assessed every hour.

Mean time to sensory onset was earlier in Dexamethasone group but was not statistically significant. Duration of motor block and sensory block were also significantly increased in dexamethasone group[2].

Hong et al, studied the effect of IV Dexamethasone in combination with caudal analgesia on post-operative pain control in seventy seven children posted for day care procedures. The patients were divided into two groups where one group received dexamethasone 0.5mg/kg followed by induction of anaesthesia. Caudal block was given with 1.5ml/kg of 0.15% ropivacaine. In the control group dexamethasone was not administered.

In the recovery room rescue analgesic consumption, pain scores and adverse effects were evaluated. Pain scores of children in Dexamethasone group were reduced significantly and only very few required rescue analgesics in recovery room. They concluded that IV Dexamethasone in doses of 0.5mg/kg in combination with caudal analgesia increased duration of analgesia and decreased the opioid consumption without any adverse effects in paediatric day care surgeries[14].

Allarasan et al,and his colleagues studied the effect of Dexamethasone in low volume supraclavicular block in 60 patients undergoing elective upper limb surgeries under ultrasound guided supraclavicular block. 60 patients were randomly divided into two groups of 30 each. The control group received 2ml of saline with 20 ml of 0.5% Bupivacaine in supraclavicular block. The Dexamethasone group received 2ml (8mg) of Dexamethasone and 20 ml of 0.5% Bupivacaine in supraclavicular block.

Duration and onset of sensory and motor block were the parameters noted. They found that in the Dexamethasone group the onset of both motor and sensory block was significantly earlier than the control group. The duration of sensory block in the Dexamethasone block was also longer and the visual analogue scales in this group after 200 minutes of block administration was lower compared the the control group.

ANATOMY OF BRACHIAL PLEXUS

The Brachial Plexus is a major network of nerves supplying the upper limb. It begins in the lateral cervical region and extends into the axilla [15]. It is formed in the posterior triangle of the neck by the union of anterior rami of fourth, fifth, sixth, seventh, eighth cervical and first thoracic spinal nerves [16]. The five roots lie behind the scalenus anterior muscle and emerge from between it and scalenusmedius to form the trunks which cross the lower part of the neck[17].The sympathetic rami carried by each root of the plexus are received from gray rami of the middle and inferior cervical rami as the roots pass between the scalenus muscles[15].

In the inferior part of the neck the roots of the brachial plexus unite to form three trunks.

- A **superior trunk** from the union of C5 and C6 roots
- A **middle trunk** which is a continuation of C7 root
- An **inferior trunk** from the union of C8 and T1 roots

Each trunk of the brachial plexus divides into anterior and posterior divisions as the plexus passes through the cervico axillary canal posterior to the clavicle**.** Anterior divisions of the trunks supply the anterior (flexor) compartments of the upper limb and posterior divisions of the trunks supply the posterior (extensor) compartments of the upper limb[15].

The divisions of the trunks form three cords of the brachial plexus

- Anterior divisions of the superior and middle trunks unite to form the **lateral cord**.
- The anterior division of the inferior trunk continues as the **medial cord**.
- Posterior divisions of all three trunks unite to form the **posterior cord.**

These three cords enter the axilla above the first part of theSubclavian artery, approach and embrace its second part giving off their branches around its third part. Thus the roots are between the scalene muscles,trunks are in the posterior triangle, divisions behind the clavicle and cords in the axilla. The brachial plexus is divided into supraclavicular and infraclavicular parts by the clavicle

The medial cord frequently receives fibres from the anterior ramus of C7. When superior root of the plexus is C4, it is called prefixed brachial plexus. When inferior root is T2 it is a post fixed brachial plexus.

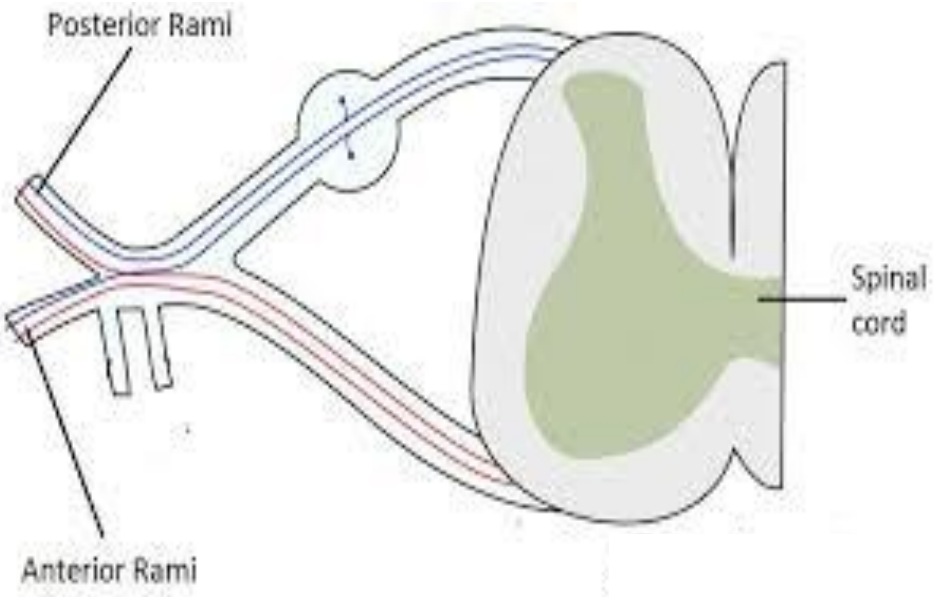


FIGURE 1: ORIGIN OF BRACHIAL PLEXUS

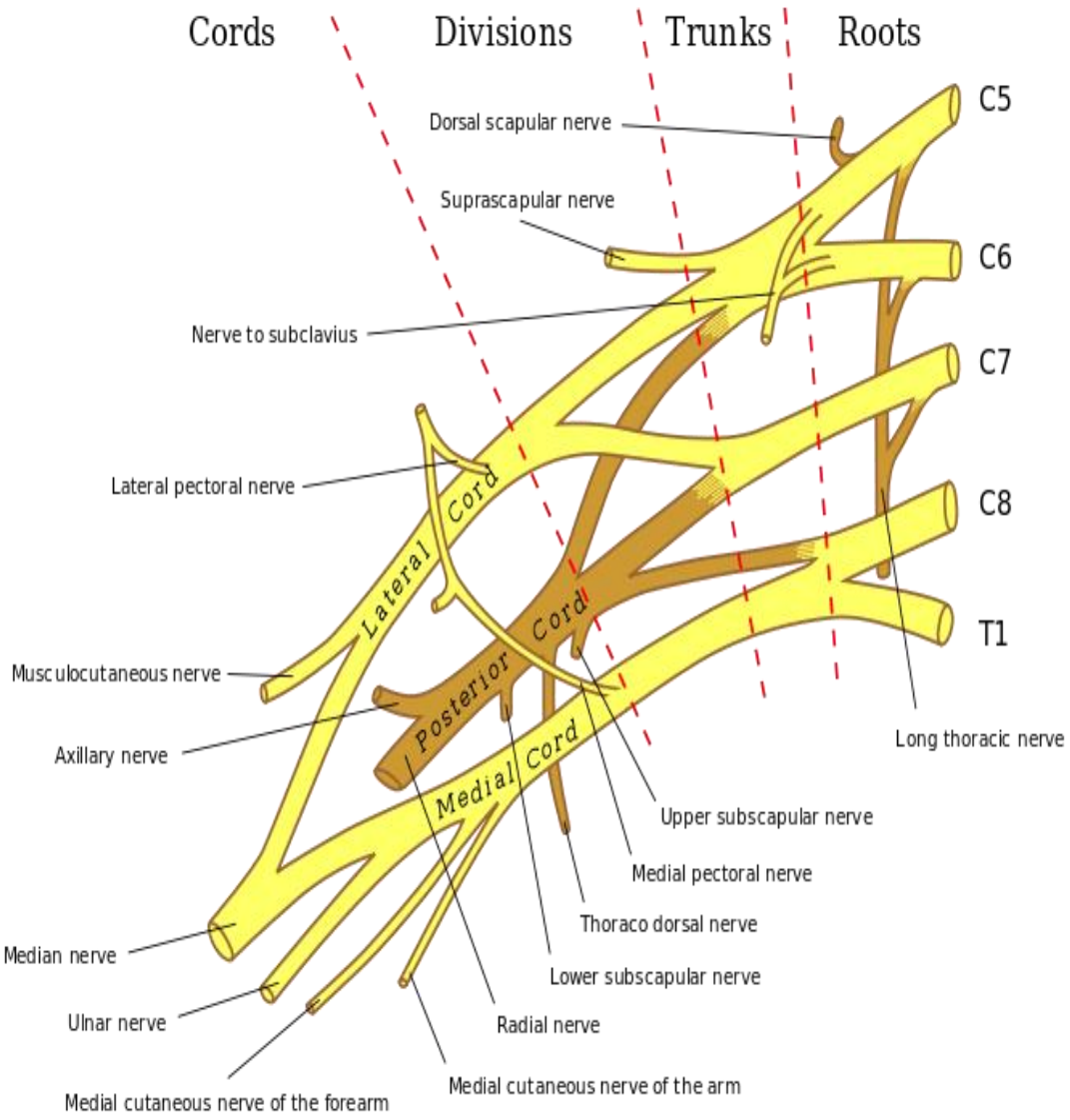


FIGURE 2 : ANATOMY OF BRACHIAL PLEXUS

Branches of different parts of the brachial plexus[17]:

Roots:

- Dorsal scapular nerve (C5)
- Long Thoracic Nerve (C5, C6,C7)
- The three Scalene (C5,C6,C7,C8),the Rhomboids (C5) and a branch to the phrenic nerve(C5)

Trunks:

- Nerve to Subclavius (C5, C6)
- Suprascapular nerve (C5,C6)

Lateral cord

- Lateral Pectoral nerve (C5,C6,C7)
- Musculocutaneous nerve (C5,C6,C7)
- Lateral root of Median nerve (C5,C6,C7)

Medial cord

- Medial pectoral nerve (C8,T1)
- Medial cutaneous nerve of arm (T1) and forearm(C8,T1)
- Ulnar nerve (C8,T1)
- Medial root of Median nerve (C8,T1)

Posterior cord

- Upper and lower scapular nerves (C5,C6)
- Thoracodorsal nerve (C5,C6,C7)
- Axillary nerve (C5,C6)
- Radial nerve (C5,C6,C7,C8,T1)

PHYSIOLOGY OF PAIN AND PAIN PATHWAYS

The international association for the study of pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[18].

Pain can be acute or chronic. Acute pain is the major reason for patients seeking medical help and is divided into nociceptive and neuropathic. Nociceptive pain result from direct activation of nociceptors in the skin or soft tissue in response to tissue injury like inflammation. Neuropathic pain result from direct injury to nerves in peripheral or central nervous system [19].

Harmful stimuli to the skin or subcutaneous tissue activate several nociceptor terminals, peripheral endings of sensory neurons whose cell bodies are located in the dorsal root ganglia and trigeminal ganglia.

Pain receptors and their stimulation:

The pain receptors in the skin and other tissues are free nerve endings. They are widespread in the superficial layers of the skin as well as in certain internal tissues like peritoneum, arterial walls, joint surfaces, the falx and tentorium in the cranial vault. Most other deep tissues are only sparsely supplied with pain endings. Mechanism by which noxious stimuli depolarize free sensory nerve endings and generate action potentials is not known. Nociceptive efferent fibres terminate predominantly in the dorsal horn of the spinal cord[20].

Pain can be elicited by multiple types of stimuli – mechanical, thermal and chemical stimuli. Fast pain is acute pain felt about 0.1 second after pain stimulus. It is elicited by mechanical and thermal types of stimuli. Slow pain begins only after 1 second of stimuli and increases slowly. It can be elicited by all three types of stimuli[19].

Some of the chemicals that excite the chemical type of pain are bradykinin, serotonin, histamine, potassium ions, acids, acetylcholine and proteolytic enzymes. In contrast to other sensory receptors pain receptors adapt very little to the various stimuli. This increased insensibility of the pain receptors is known as hyperalgesia. The intensity of pain is also closely correlated with the rate of tissue damage from causes other than heat such as bacterial infections, tissue ischemia, contusion and so on. The intensity of the pain felt correlates with the local increase in potassium ion concentration or theproteolytic enzymes that directly attack the nerve endings and excite pain by making the nerve membranes more permeable to ions.

When blood flow to a tissue is blocked, the tissue often becomes very painful within a few minutes. One of the suggested causes of pain during ischemia is accumulation of large amounts of lactic acid in the tissues formed as a consequence of anaerobic metabolism[20].

Pain Pathways[20]:

Even though all pain receptors are free nerve endings, they use two separate pathways – the **Neospinothalamic tract** for the fast pain and the **Paleospinothalamic tract** for chronic pain.

The fast sharp pain signals are elicited by either mechanical or thermal pain stimuli. They are transmitted in the peripheral nerves to the spinal cord by small type A∂ fibers at velocities between 6 and 30m/sec. The slow chronic pain is transmitted to the spinal cord by C type fibers at velocities between 0.5 and 2m/sec.

Because of this dual system of pain innervation, a sudden painful stimulus often gives a 'double' pain – the sharp and the slow pain. The former warns the person of the damaging influence while the latter tends to increase over time and makes the person keep trying to relieve the cause of pain.

On entering the spinal cord from the dorsal spinal roots, the pain fibres terminate on relay neurons in the dorsal horns. Here again there are two systems for processing the pain signals on their way to the brain.

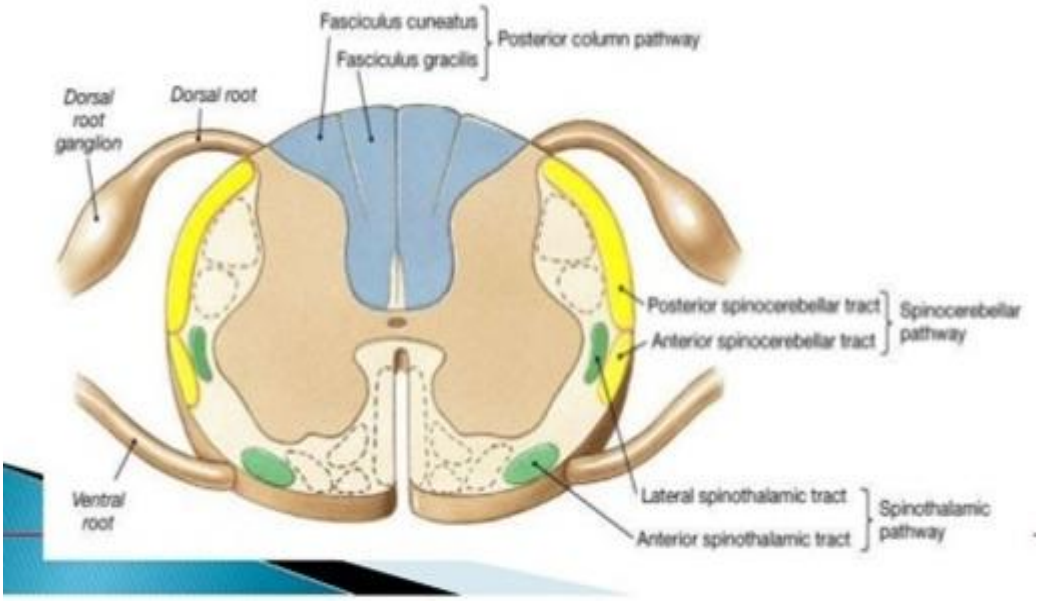


FIGURE 3: PAIN TRACTS IN SPINAL COLUMN

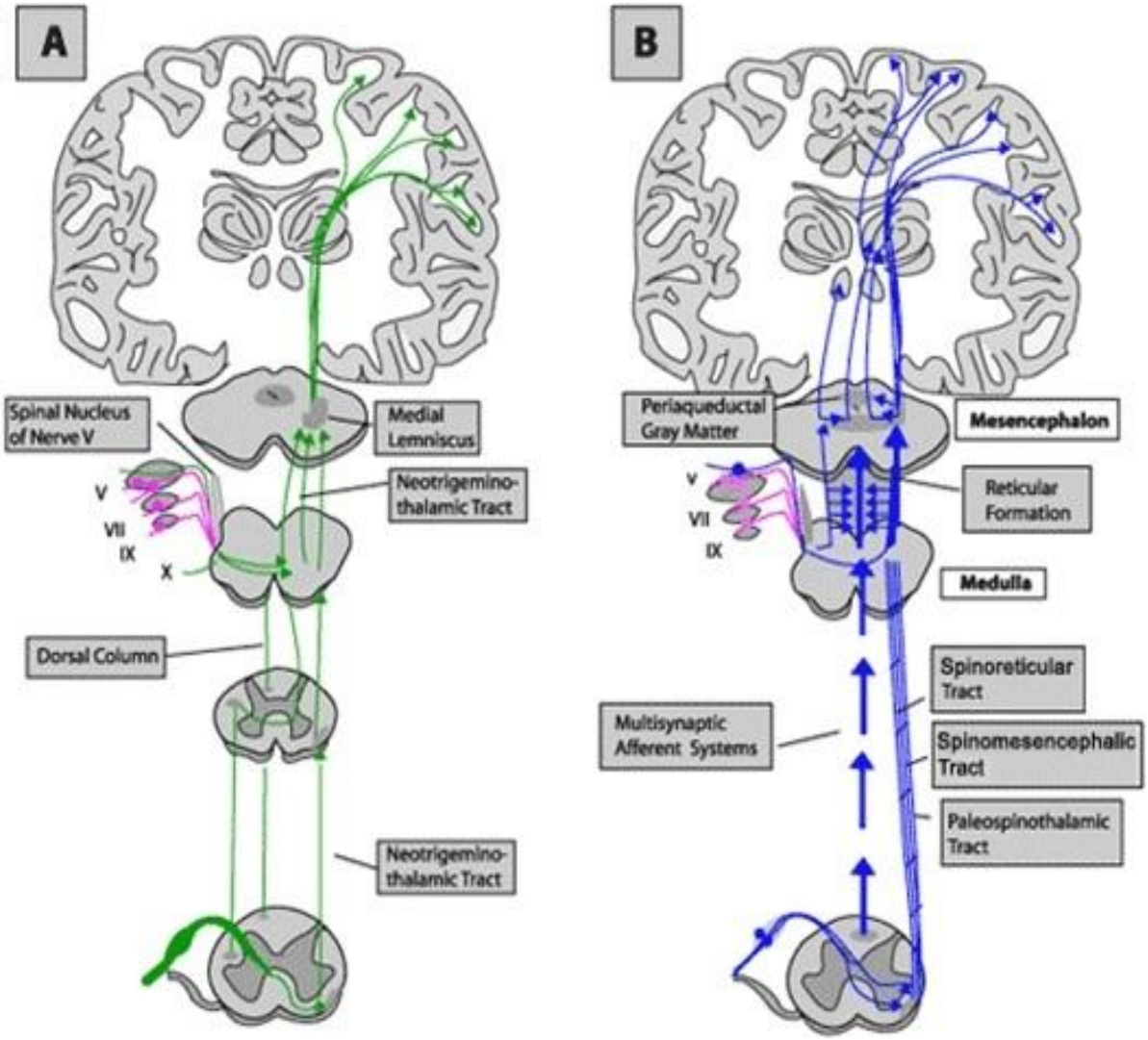


FIGURE 4: PAIN PATHWAYS

Neospinothalamic tract for fast pain

The fast type A∂ fibers transmit mechanical and acute thermal pain terminating in **lamina I** (LAMINA MARGINALIS) of the dorsal horns. Later they excite second order neurons of the neospinothalamic tract. These give rise to long fibres that cross immediately to the opposite side of the cord through the anterior commissure and then passing upward to the brain in the antero lateral columns**. Glutamate**is the neurotransmitter of the A∂ fibres.

A few fibres of the neospinothalamic tract terminate in the reticular areas of the brain stem, but most pass to the thalamus without interruption, terminating in the ventrobasal complex along with the dorsal column- medial lemniscal tract for tactile sensations. A few fibers also terminate in the posterior nuclear group of the thalamus. From thalamus the signals are transmitted to other basal areas of the brain and to the somatosensory cortex.

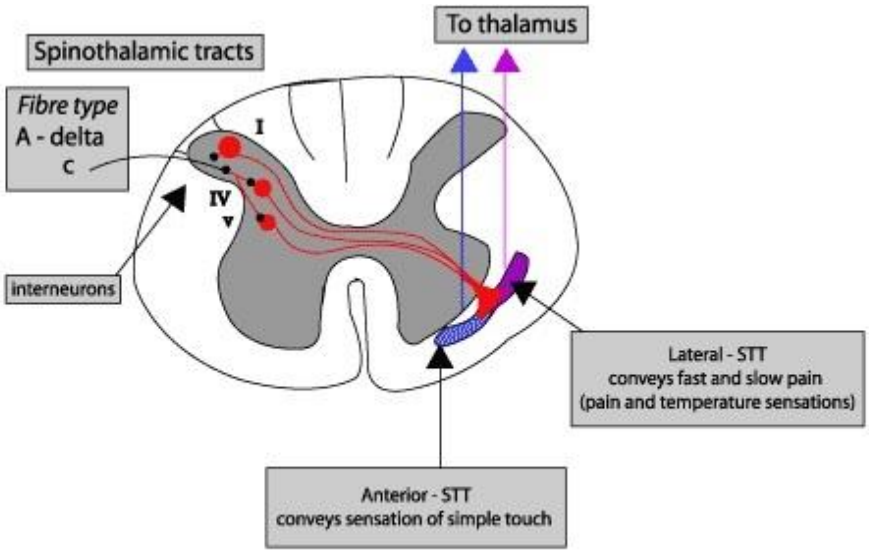


FIGURE 5: FAST AND SLOW PAIN PATHWAYS

Paleospinothalamic tract for slow chronic pain:

This transmits pain from the slow chronic type C pain fibers and some signals from type A∂ fibres also. The peripheral fibers terminate in the spinal cord almost entirely in laminae II and III of the dorsal horns, which together are called the **substantia gelatinosa** .Most of the signals then pass through one or more additional short fibre neurons within the dorsal horns themselves before enteringlamina V. Here the last neurons in the series give rise to long axons that mostly join the fibres from the fast pain pathway. They pass through the anterior commissure to the opposite side of the cord, then upward to the brain in the anterolateral pathway. Type C pain fibers release both **glutamate** and **substance P** transmitters.

The slow chronic pathway terminates widely in the brain stem. Only one tenth to one fourth of the fiberspassto the thalamus. Most terminate in either of the three areas:

(1) the reticular nuclei of the medulla, pons and mesencephalon

(2) the tectal area of the mesencephalon to the superior and inferior colliculi

(3) the peri –aqueductal gray region surrounding the aqueduct of Sylvius.

From here multiple short fiber neurons relay the pain signals upward into the intralaminar and ventrolateral nuclei of the thalamus and into certain portions of the hypothalamus and other basal areas of the brain.

TABLE 1 : NERVE FIBRES IN PAIN TRANSMISSION

A FIBRES		C FIBRES
A – BETA FIBRES	**A – DELTA FIBRES**	
➢ Large ➢ Myelinated ➢ Fast conducting ➢ Low stimulation threshold ➢ Respond to light touch	➢ Small ➢ Lightly Myelinated ➢ Slow conducting ➢ Respond to heat pressure, cooling & chemicals ➢ Sharp sensation of pain	➢ Small ➢ Unmyelinated ➢ Very slow conducting ➢ Respond to all types of noxious stimuli ➢ Transmit prolonged dull pain ➢ Require high intensity stimuli to trigger a response

STRUCTURE AND BIOSYNTHESIS OFADRENOCORTICAL HORMONES

The hormones of the adrenal cortex are derivatives of cholesterol and hence contain the Cyclopentanophenanthrenenucleus. Gonadal and adrenocortical steroids are of three types :

- C_{21} steroids with two- carbon side chains at position 17,
- C_{19} steroids which have keto or hydroxyl group at position 17 and
- C_{18} steroids which in addition to a 17 keto or hydroxyl group, have no angular methyl group attached to position 10.

The adrenal cortex secretes primarily C_{21} and C_{19} steroids[21].

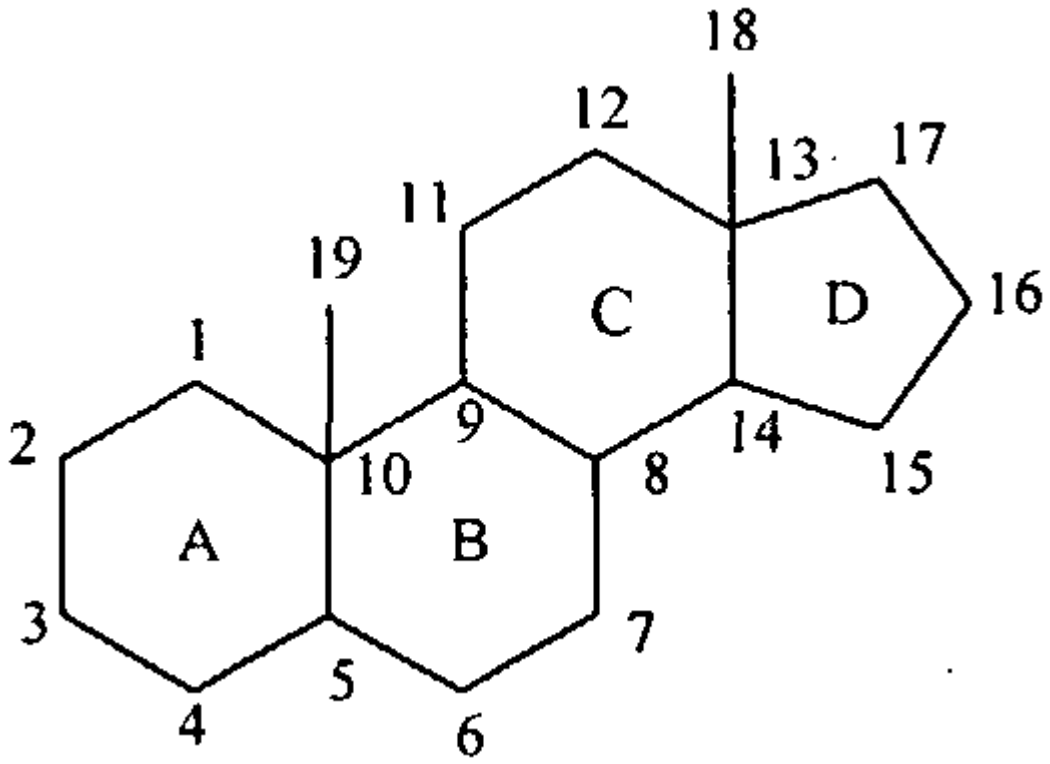


FIGURE 6: CYCLOPENTANOPHENANTHRENE RING

STEROID BIOSYNTHESIS:

The precursor of all steroids is cholesterol. Some of the cholesterol is synthesized from acetate but most of it is taken up from circulating low density lipoprotein (LDL). LDL receptors are abundant in adrenocortical cells. Cholesterol ester hydrolase catalyzes the esterification of free cholesterol in lipid droplets and is transported to mitochondria by a sterol carrier protein. Here it is converted to pregnenolone a reaction catalyzed by a side chain cleavage enzyme known as cholesterol desmolase[22].

Pregnenolone moves to the smooth endoplasmic reticulum where some of it is dehydrogenated to form progesterone with the help of 3βhydroxysteroid dehydrogenase. Conversion of 17αhydroxypregnenolone to 17αhydroxyprogesterone and dehydroepiandrosterone to androstenidione is also done by this enzyme. 17αhydroxylase catalyzes the formation of 17α hydroxypregnenolone and 17αhydroxyprogesterone from pregenolone and progesterone respectively. Hydroxylation of progesterone to 11-deoxycorticosterone and17αhydroxyprogesterone to 11-deoxycoticostrerol is catalyzed by 21β hydroxylase in the smooth endoplasmic reticulum[21].

11-deoxycorticosterone and 11-deoxycortisol move back to the mitochondria where they are 11- hydroxylated to form corticosterone and cortisol. These reactions are catalyzed by 11-β hydroxylase and takes place in the zonafasiculata and zonareticularis.

In the zona glomerulosa aldosterone synthetase helps in in the formation of aldosterone.

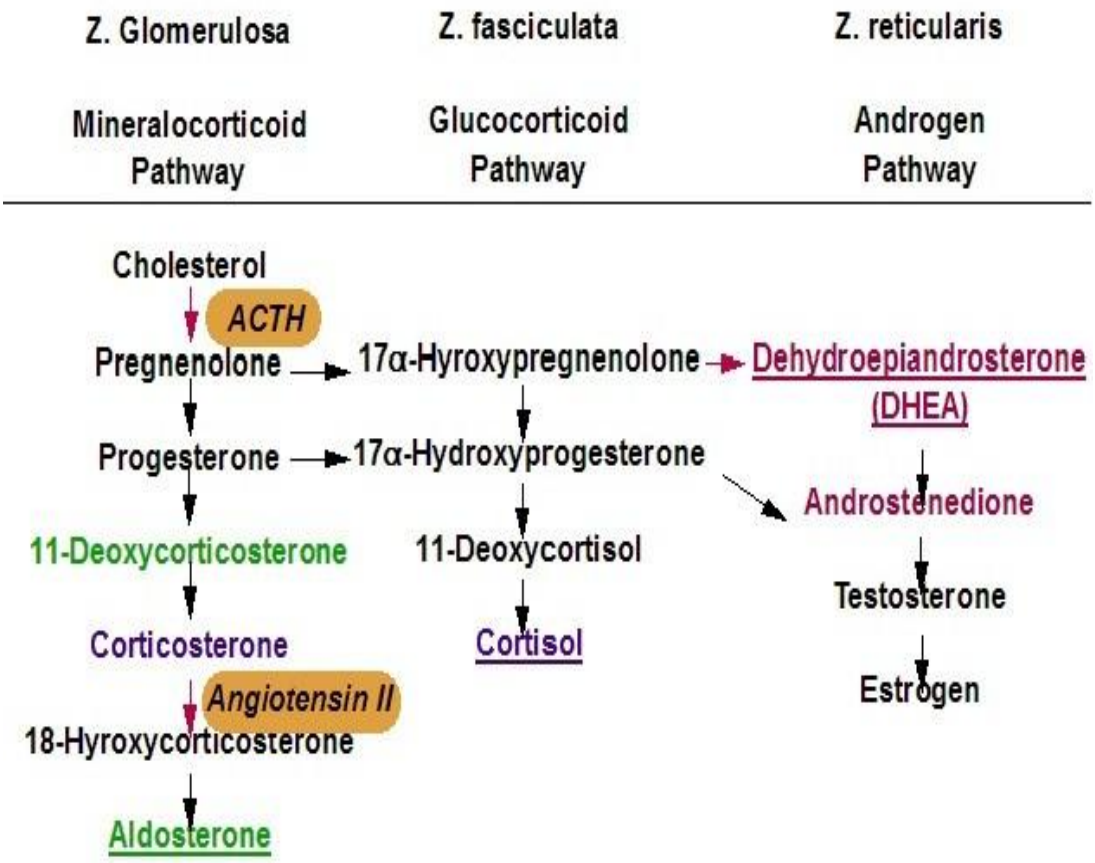


FIGURE 7: PATHWAYS OF ADRENAL STEROID BIOSYNTHESIS INADRENAL CORTEX

METABOLISM AND EXCRETION OF GLUCOCORTICOIDS:

Cortisol is metabolized in the liver which is the principal site of glucocorticoid metabolism. Most of the cortisol is reduced to dihydrocortisol and then to tetrahydrocortisol, which is conjugated to glucuronic acid. The liver and other tissues contain the enzyme 11βhydroxysteroid dehydrogenase which occurs in two forms. Type 1 catalyzes the conversion of cortisol to cortisone and the reverse reaction. Type 2 catalyzes almost exclusively the one way conversion of cortisol to cortisone.Cortisol is an active glucocorticoid and is not secreted in appreciable quantities by the adrenal glands. Very little of the cortisone formed in the liver enters the circulation because it is promptly reduced and conjugated to form tetrahydrocortisone glucuronide. These are freely soluble, enter the circulation and are rapidly excreted in the urine since they are not bound to proteins.

There is an entero-hepatic circulation of glucocorticoids and about 15% of the secreted cortisol is excreted in the stools[21].

PHYSIOLOGICAL FUNCTION AND PHARMACOLOGICAL ACTIONS:

Adrenal cortex releases a large number of steroids into the circulation. Some have minimum biological activity and function primarily as precursors and there are some with no function. Hormonal steroids are classified as those having important effects on intermediary metabolism and Immune function –

- glucocorticoids C_{21}, hormones having primarily salt retaining activity
- mineralocorticoids C_{21} and
- those having androgenic or estrogenic activity C_{19}

In humans the major glucocorticoid is cortisol and most important mineralocorticoid is aldosterone [22].

Corticosteroids and their biologically active synthetic derivatives are employed at physiological doses for replacement therapy when endogenous production is impaired. Glucocorticoids potently suppress inflammation and their use in a variety of inflammatory and autoimmune diseases makes them the most prescribed classes of drugs. Since they exert effects on almost all organ systems the clinical use and withdrawal from corticosteroids are complicated by a number of side effects, some of which are life threatening [23].

Corticosteroids have numerous widespread effects which includes alteration in carbohydrate, protein and lipid metabolism, fluid and electrolyte balance,maintenance and preservation of normal function of cardiovascular system, immune system, kidney, skeletal muscle, endocrine and nervous system. They help the organism to resist stressful circumstances like noxious stimuli and environmental changes.

PHYSIOLOGIC EFFECTS:

Major metabolic consequences of glucocorticoid secretion are due to direct action of these hormones in the cell. Some important effects are result of

homeostatic responses by insulin and glucagon. Most effects of glucagon are dose related and are increased greatly when large amounts are administered for therapeutic purposes. At the same time there are other effects called permissive effects without which many normal functions becomes deficient[22].

METABOLIC EFFECTS:

Glucocorticoids have dose related effects on carbohydrate, protein and fat metabolism. They are required for gluconeogenesis and glycogen synthesis in the fasting state. They stimulate enzymes responsible for release of amino acids in the course of muscle metabolism. Glucocorticoids stimulate insulin release by increase in serum glucose levels and inhibit uptake of glucose by muscle cells. They stimulate hormone sensitive lipase and thus cause lipolysis. The increased insulin secretion stimulates lipogenesis and also inhibits lipolysis leading to a net increase in fat deposition combined with increased release of fatty acids and glycerol into the circulation[23].

CATABOLIC AND ANTI ANABOLIC EFFECTS:

Though glucocorticoids stimulate RNA and protein synthesis in liver, they have catabolic and anti-anabolic effects in lymphoid and connective tissue, muscle, peripheral fat and skin. Increased levels of the hormonecauses decreased muscle mass, weakness and thinning of the skin. Catabolic effect on bones causes osteoporosis. In children they reduce growth which may be partially prevented by administration of growth hormone in high doses[23].

ANTI-INFLAMMATORY AND IMMUNOSUPPRESSIVE EFFECTS:

Glucocorticoids considerably reduce inflammation by their peripheral effects on the concentration, distribution and function of peripheral leukocytes and suppressive effects on the inflammatory cytokines, chemokinesand other mediators of inflammation. The extravasation and infiltration of leukocytes seen in inflammation is mediated by a complex series of interactions of white cell adhesion molecules with those on endothelial cells and are inhibited by glucocorticoids.

Glucocorticoids also inhibit the function of tissue macrophages and other antigen presenting cells. It limits the ability of the macrophages to phagocytose and kill microorganisms and to produce tumour necrosis factor **α interleukin-I,** metalloproteinases and plasminogen activators. Glucocorticoids also influence inflammatory response by reducing the prostoglandin, leukotriene and platelet activating factor synthesis that result from activation of phospholipase A_2[22,23].

Glucocorticoids suppresses the mast cell degranulation causing vasoconstriction when applied directly to the skin. By reducing amount of histamine released by basophils and mast cells they also decrease capillary permeability.

OTHER EFFECTS:

Glucocorticoids have important effects on the nervous system. Increased amounts produce behavioral disturbances in humans like insomnia, euphoria and finally depression. Large doses increase the intracranial pressure. When given chronically they suppress release of pituitary hormones likeadreno-coticotrophichormone(ACTH), growth hormone, thyroid stimulating hormone(TSH) and lutenising hormone. Large doses are also associated with formation of peptic ulcerand fat redistribution in the body.

Cortisol deficiency causes impaired renal function, augments vasopressin secretion and diminishes ability to excrete water load.

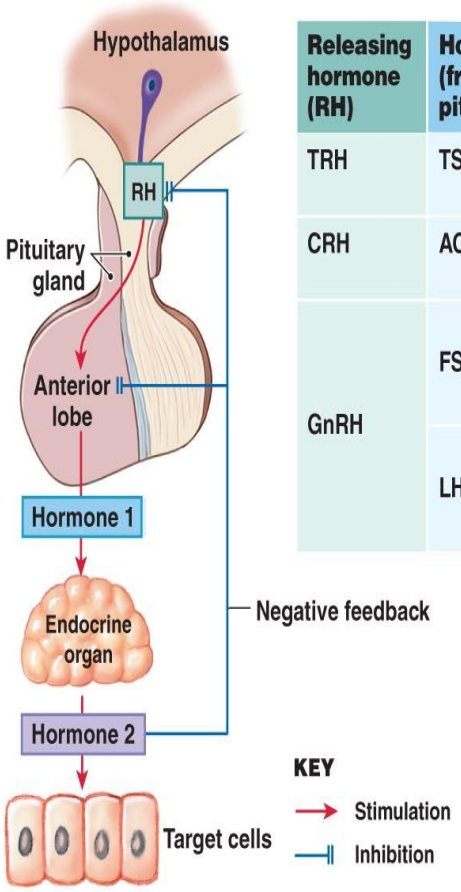
They play an important role in the development of fetal lung[22,23].

Regulation of glucocorticoid secretion:

Both basal secretion of glucocorticoids and the increased secretion by stress are dependent on ACTH from the anterior pituitary. ACTH produces prompt increase in glucocorticoid secretion and also sensitizes the adrenal to subsequent doses of ACTH. ACTH is secreted in irregular bursts throughout the day and plasma cortisol tends to rise and fall in response to these bursts. In humans, the bursts are most frequent in the early morning and hence about 75% of the daily production of cortisol occurs between 4 AM to 10AM. The bursts are less frequent in the evening. The biologic clock responsible for the diurnal ACTH rhythm is located in the suprachiasmatic nuclei of the hypothalamus.

Free glucocorticoids inhibit ACTH and the degree of pituitary inhibition is proportional to the circulating glucocorticoid level. The inhibition occurs at both pituitary and hypothalamic levels. The inhibition is primarily due to its action on DNAand maximal inhibition takes several hours to develop.The ACTH inhibiting activity of the steroid hormones parallels their glucocorticoid potency. When prolonged treatment with anti-inflammatory doses of glucocorticoid is stopped, the adrenal is atrophic and unresponsive. Its responsiveness is restored by injecting ACTH and the pituitary may take nearly a month to secrete physiologic levels of cortisol.The complications of sudden cessation of steroid therapy can be avoided by tapering the steroid dose over a long period of time[21].

The control of hypothalamic and pituitary hormone secretion by negative feedback



Releasing hormone (RH)	Hormone 1 (from pituitary)	Endocrine target organ	Hormone 2 (from target organ)
TRH	TSH	Thyroid gland	Thyroid hormones
CRH	ACTH	Adrenal cortex	Gluco-corticoids
GnRH	FSH	Testes	Inhibin
		Ovaries	Inhibin, Estrogens
	LH	Ovaries	Progestins, Estrogens
		Testes	Androgens

FIGURE 8: REGULATION OF GLUCOCORTICOID SECRETION

SYNTHETIC CORTICOSTEROIDS:

The need for development of many synthetic steroids with similar actions to glucocorticoids has increased considerably since glucocorticoids have become important agents for use in the treatment of many inflammatory, immunologic, hematologic and other disorders. These are synthesized from cholic acid obtained from cattle or steroid sapogenins found in plants. Synthetic corticosteroids are in most cases rapidly and completely absorbed when given by mouth. Although they are transported and metabolized similar to that of endogenous steroids important differences exist between these synthetic steroids. They have different ratios of glucocorticoid to mineralocorticoid potency.

TABLE 2: RELATIVE POTENCIES AND EQUIVALENT DOSES OFREPRESENTATIVE CORTICOSTEROIDS

COMPOUND	ANTI-INFLAMMATORY POTENCY	SODIUM RETAINING POTENCY	DURATION OF ACTION	EQUIVALENT DOSE(mg)
Cortisol	Intermediate	Intermediate	Short	20
Cortisone	0.8	0.8	Short	25
Fludrocortisone	10	125	Intermediate	Not used for glucocorticoid activity
Prednisone	4	0.8	Intermediate	5
Prednisolone	4	0.8	Intermediate	5
6αMethylprenisolone	5	0.5	Intermediate	4
Triamcinalone	5	0	Intermediate	4
Betamethasone	25	0	Long	0.75
Dexamethasone	25	0	Long	0.75

PHARMACOLOGY OF DEXAMETHASONE

Glucocorticoids, natural and synthetic are adrenocortical steroids readily absorbed from gastrointestinal tract. They cause varied metabolic effects in addition to modifying the body's immune system to diverse stimuli.

Dexamethasone is a long acting, high potency synthetic analogue of glucocorticoids and is primarily used for its anti-inflammatory effects in disorders of many organ systems. At equipotent anti-inflammatory doses, Dexamethasone almost completely lacks the sodium retaining property of Hydrocortisone and its closely related derivatives. In addition to binding specific nuclear steroid receptors, it interferes with nuclear factor kappa B pathway activation[23].

Dexamethasone increases regional block associated analgesia due to either inhibitory activity of potassium channels on pain sensitive sensory neurons or by producing vasoconstriction. Use of Dexamethasone as an adjuvant to local anaesthesia has been widely investigated[24].

Structure:

Dexamethasone is a 9 -Fluoro-Glucocorticoid

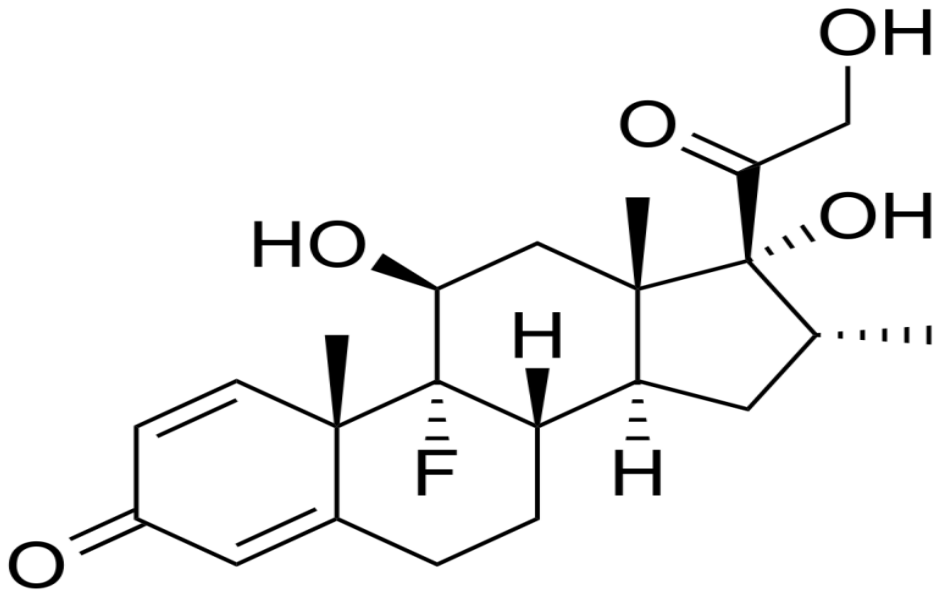


FIGURE 9: DEXAMETHASONE CHEMICAL STRUCTURE

Absorption:

Dexamethasone is rapidly and almost completely absorbed when given in the oral route. When given intramuscularly the freely soluble esters like sodium phosphate and sodium succinate are rapidly absorbed. The poorly soluble esters like acetate, diacetate and so on are slowly but completely absorbed. Absorption of local application of Dexamethasone is less rapid than intramuscular injection. Biological half life of Dexamethasone is 36 to 54 hours[24].

Mechanism of action:

Dexamethasone is a glucocorticoid agonist. Unbound Dexamethasone crosses cell membranes and binds with high affinity to specific cytoplasmic glucocorticoid receptors. This complex binds to DNAelements (glucocorticoid response elements) which results in a modification of transcription, altered protein synthesis to achieve inhibition of leukocyte infiltration at the site of inflammation, interference in the function of mediators of inflammatory response, suppression of humoral immune responses and reduction in oedema or scar tissue. The anti inflammatory actions of Dexamethasone are thought to involve phospholipase A_2 inhibitory proteins –lipocortins which control the biosynthesis of potent mediators of inflammation like prostaglandins and leukotrienes.

Dexamethasone has been shown to exhibit anaesthetic, anti – enetic anti-microbial, appetite stimulant, muscle binding and sedative functions .Its

potency is about 20 to 30 times that of Hydrocortisone and 4to 5 times of Prednisone[25].

Dexamethasone in nerve blocks:

Exact mechanism of Dexamethasone action in prolonging blocks is not known but its addition can considerably prolong duration of analgesia with minimal adverse effects . It is thought that Dexamethasone may prolong block duration by increasing activity of inhibitory potassium channels on nociceptive C fibres[26,27]or by causing vasoconstriction via glucocorticoid receptor mediated nuclear transcription modulation[28]. Suppression of inflammatory mediators including prostaglandins (PGE_2) may also play a role.

The possible analgesic mechanism of IV Dexamethasone is that they activate cytoplasmic glucocorticoid receptors which bind to glucocorticoid response elements in DNA[29]. This leads to decreased production of inflammatory proteins and increased production of anti-inflammatory proteins[12,13,30].

LOCAL ANAESTHETICS

Local anaesthetics are drugs which provide anaesthesia and analgesia for various surgical procedures [31]. They are also used in management of chronic pain and treatment of cardiac arrhythmias. Local anaesthetics produce reversible conduction blockade of impulses along central and peripheral nerve pathways[32].

The first local anaesthetic Cocaine was introduced in 1884 by Karl Koller for use in Ophthalmology. The first synthetic local anaesthetic was the ester derivative Procaine introduced by Einhorn in 1905. Lidocaine was synthesised as an amide local anaesthetic in 1943 by Lofgren[33].

MOLECULAR STRUCTURE:

Local anaesthetics are weak bases that are poorly soluble in water. They are marketed as water soluble salt of an acid (mostly hydrochloric acid).

- They contain a lipophilic and a hydrophilic portion separated by a hydrocarbon chain.
- The hydrophilic group is a tertiary amine and the lipophilic group is an unsaturated aromatic ring.
- The anaesthetic effect of the drug is from the lipophilic portion of the drug[31].

CLASSIFICATION:

Local anaesthetics are mainly classified based on their structure into:

- Amide local anaesthetics:-

Lidocaine, Prilocaine, Bupivacaine, Ropivacaine, Levobupivacaine, Mepivacaine

- Ester local anaesthetics:-

Procaine, Chlorprocaine, Tetracaine

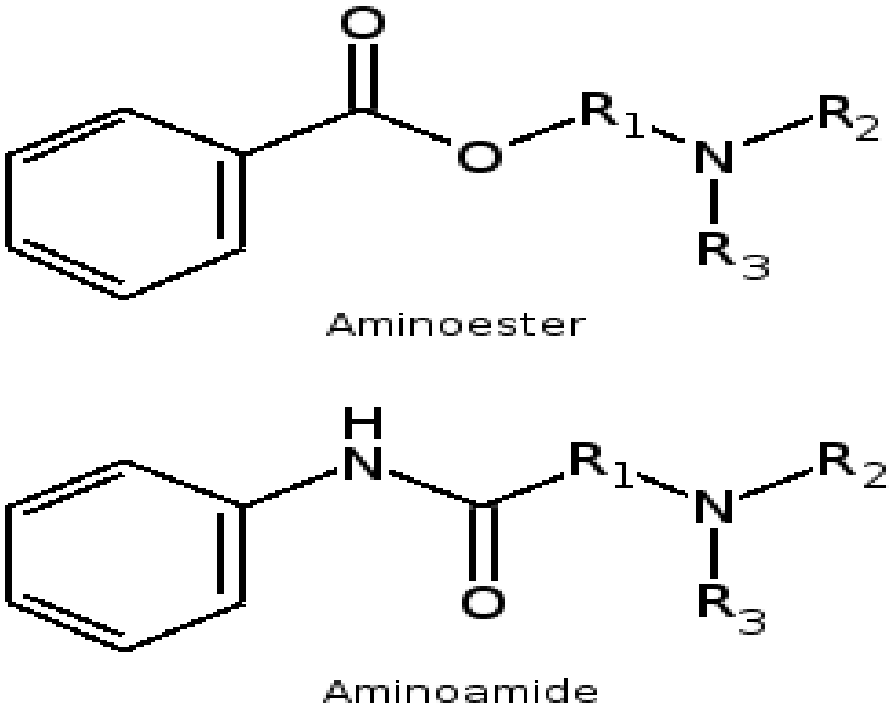


FIGURE 10 : STRUCTURE OF ESTER AND AMIDE LOCAL ANAESTHETIC

BUPIVACAINE HYDROCHLORIDE:

$C_{18}H_{28}N_2o$, HCl

(±) –1–Butyl–N–(2,6–dimethyl phenyl)–2– piperidine–carboxamide.

It was synthesized in 1957 by B. Ekenstam

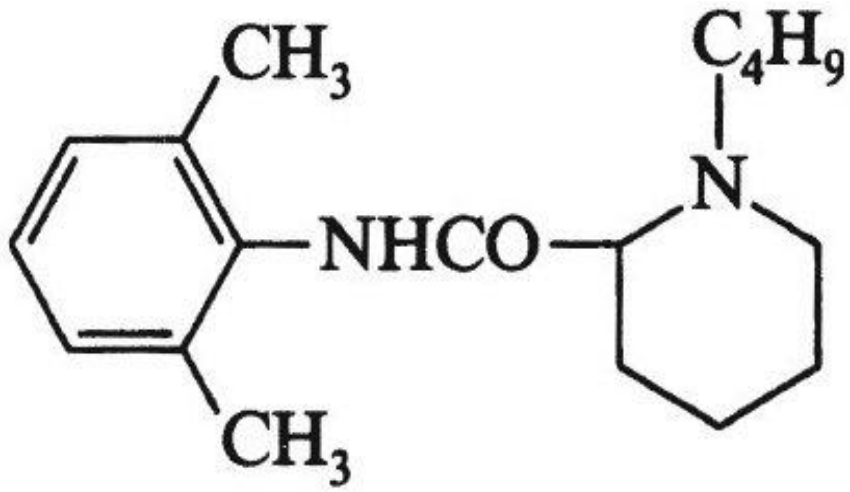


FIGURE 11: STRUCTURE OF BUPIVACAINE

PHYSIOCHEMICAL PROPERTIES[25]:

Molecular weight - 288

pKa - 8.1

Lipid solubility - 30

Partition coefficient (octanol /buffer) – 3,460

Protein binding - 95%

Bupivacaine hydrochloride is a white, odourless, crystalline powder with a bitter, numbing taste. It is prepared by chemical synthesis. The hydrochloride salt is available in solution. Bupivacaine used for peripheral nerve blocks contain preservative Methylparaben. Bupivacaine used for spinal anaesthesia is usually preservative free and contains dextrose to make it hyperbaric.

MECHANISM OF ACTION:

Bupivacaine prevents the transmission of the nerve impulses by inhibiting passage of sodium ions through ion- selective sodium channels in nerve membranes. Sodium channel itself is a specific receptor for local anaesthetic molecule. Failure of sodium ion channel permeability to increase, slows the rate of depolarization. Hence threshold potential is not reached and thus an action potential is not propagated[34].

BUPIVACAINE TOXICITY:

i.) Cardiovascular system toxicity:

Bupivacaine is a potent cardiac depressor compared to other local anaesthetic drugs. It depresses the rapid phase of depolarization in the purkinjeefibres and the ventricles. It also decreases the action potential duration and the effective refractory period.

Electrophysiologic studies have shown that high blood levels of the drug will prolong conduction time through various parts of the heart. Bupivacaine exerts a dose dependent negative ionotropic action on the cardiac muscle[35].

It also depresses the myocardial contractility by affecting the influx of calcium and triggered release from the sarcoplasmic reticulum[36].

ii.) Central nervous system toxicity:

In bupivacaine toxicity the central nervous system (CNS) manifestations occur secondary to cardiac manifestations. Initial symptoms include feeling of light headedness and dizziness followed by visual and auditory disturbances such as tinnitus and difficult focussing. Other symptoms of CNS toxicity includes shivering, muscle twitches, tremors, disorientation and occasional feeling of drowsiness. Effects on the CNS may be the result of an initial blockade of inhibitory pathways in the cerebral cortex by local anaesthetics. At still higher doses of the drug excitation is followed by CNS depression, hypoventilation, respiratory arrest and generalised convulsions[32,33,34].

PHARMACOKINETICS:

i.) Absorption:

Absorption of local anaesthetic from its site of injection into the systemic circulation is influenced by site of injection, dosage, use of Epinephrine and pharmacologic characteristics of drug[32] .

ii.) Distribution:

More highly perfused organs are responsible for initial rapid uptake (α phase) which is followed by a slower distribution (β phase) to moderately perfused tissues. First pass pulmonary extraction of Bupivacaine is dose dependent, suggesting that uptake process becomes saturated rapidly. Muscle provides the greatest reservoir for the drug because of its large mass .

Distribution characteristics:

1. $T_{1/2}$ – 21 minutes
2. Volume of distribution at steady state – 73 litres
3. Clearance (Litre/minute) – 0.58

iii.) Biotransformation and excretion:

Bupivacaine undergoes metabolism by aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation in the liver.

Only the N-dealkylated metabolite, N-desbutyl bupivacaine has been measured in blood or urine after administration of the drug .

The excretion occurs via the kidney. Less than 5 % of unchanged drug is excreted via the kidney through urine[33].

DOSE:

The maximum allowable dose is 3 mg/ kg body weight. It is available as 0.5% and 0.25% solution containing 5mg/ml and 2.5mg/ml of Bupivacaine respectively[31,32,33,34].

SUPRACLAVICULAR BLOCK

Supraclavicular block was first performed by Kulenkampff on himself in Germany in 1911[37].

It is often referred to as the spinal anaesthesia of the upper extremity because of its ubiquitous application in upper limb surgeries. The block is performed at the level of distal trunks and origin of divisions. At the lateral border of anterior scalene muscle the Brachial Plexus passes down between the first rib and clavicle to enter the axilla. The trunks are tightly oriented vertically on top of the first rib just posterior to the Subclavian artery. The Brachial plexus is very compact here and hence it blocks all the nerves of the Brachial Plexus achieving excellent anaesthesia of forearm and hand[38,39].

The Supraclavicular block results in anaesthesia of dermatomes C5 to T1 and makes it a suitable technique to provide anaesthesia and analgesia of the entire upper limb distal to the shoulder[38,39].

INDICATIONS:

i. Anaesthesia for procedures involving the upper arm, forearm and hand.

CONTRAINDICATIONS:

i. Patient refusal
ii. Local infection at the site of injection
iii. Pre-existing peripheral neuropathies

TECHNIQUES[40]:

Supraclavicular block can be mainly done by three methods:

- Blind technique or the paresthesia technique
- Nerve stimulator guided block
- Ultrasound guided block

BLIND (or) PARESTHESIA TECHNIQUE:

This is the most straightforward and easiest techniques used and is referred to as the "**BROWN & BRIDENBAUGH'S PLUMB-BOB TECHNIQUE**".

The patient is placed in the supine position without pillow and head is turned to the contralateral side. The lateral border of sternocleidomastoid is identified and palpated. Needle entry point is at the posterior border of the muscle just above the clavicle. The needle is directed towards the floor and advanced till paraesthesia or muscle contraction of the forearm is noted. The first rib acts as the medial barrier to the needle's entry point[40].

Once the plexus is identified, 1-2 ml of the local anaesthetic solution is given to rule out intravascular or intrathecal injection and then is followed by fractionated injection of the local anaesthetic[38].

The second method is to palpate the interscalene groove at its most inferior point just posterior to the subclavian pulse in a plane just medial to the

midpoint of the clavicle and to inject the local anaesthetic after paresthesia is experienced by the patient[38].

FIGURE 12: TECHNIQUE OF SUPRACLAVICULAR BLOCK

NERVE STIMULATOR TECHNIQUE:

Needle used for nerve stimulator technique are polymer coated insulated 24 to 26 gauge needles measuring about 5-10 cm. The bevel point in such needles are designed to minimize trauma to nerves and maximize tactile sensitivity during needle placement.

The patient is placed in the supine position with the head turned to the contralateral side. The plexus is first palpated lateral to the sternocleidomastoid muscle. Needle insertion point is located immediatelycephalad to the palpating finger. The needle is inserted almost in a perpendicular direction to the skin in slight caudal direction. The upper trunk is identified by twitching of the shoulder muscles. The needle is advanced till motor response is elicited in the forearm and hand at the set current. Motor response should be sustained at a current below 0.5 mA after which the local anaesthetic is injected after aspiration [37,38].

ULTRASOUND GUIDED BLOCKADE:

Patient is placed in supine position and head is turned to the opposite direction. A linear high frequency probe is placed in the supraclavicular regionand directed towards the thorax. The Subclavian artery is identified first and the Brachial plexus appears as multiple hypoechoic discs lateral & superficial to the artery. The first rib is seen as a hyperechoic mass deep to the artery and pleura is identified by its movement on breathing next to the rib[38,40].

IN- PLANE TECHNIQUE:

A short blunt tipped 22 gauge needle is used. Needle is inserted cephalad to the ultrasound probe in a posterior and caudal direction. The local anaesthetic solution is injected in increments of 5 ml after careful aspiration[43].

OUT OF PLANE TECHNIQUE:

A longer needle is commonly used. The needle is inserted just lateral to the probe parallel to the ultrasound beam and is medially advanced towards the Subclavian artery till the tip is visualized near the plexus just lateral and above the artery. After careful aspiration the local anaesthetic is injected in small increments at variable points which should be visualized surrounding the plexus[43,44,45].

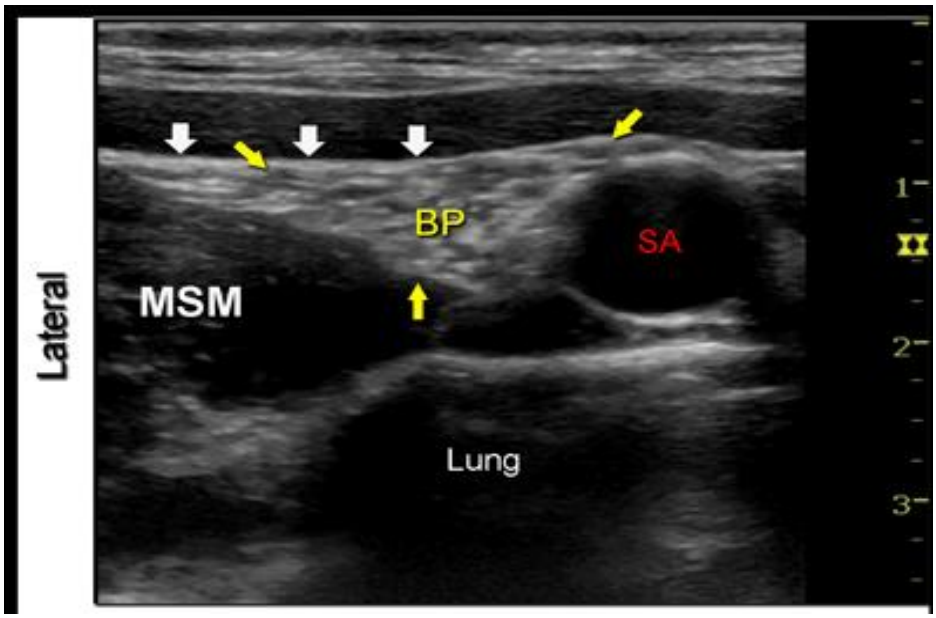


FIGURE 13: SONOANATOMY OF BRACHIAL PLEXUS

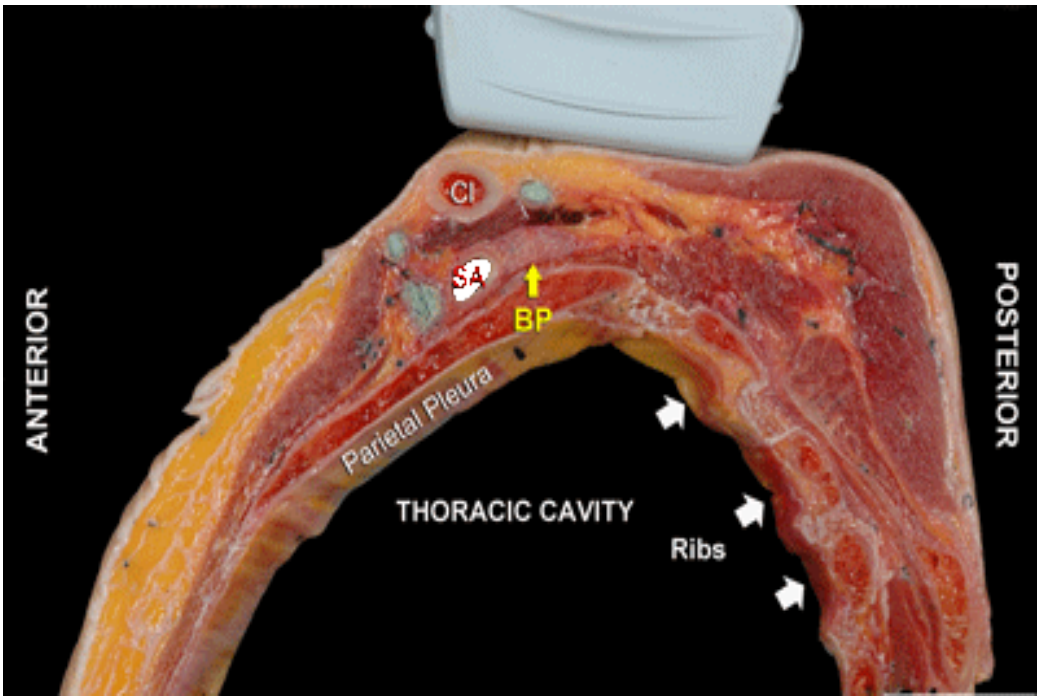


FIGURE 14: CROSS SECTION OF STRUCTURES SEEN IN ULTRASOUND

FIGURE 15: ULTRASOUND GUIDED SUPRACLAVICULAR BLOCK

COMPLICATIONS[37,38,39]:

i. Pneumothorax

ii. Phrenic nerve paralysis

iii. Injury to the nerve fibers

iv. Inadvertent arterial puncture

v. Inadvertent intrathecal puncture

vi. Local anaesthetic systemic toxicity

METHODOLOGY

The study was done in **PSG Institute of Medical sciences & Research, Coimbatore** during the period 01/07/2016 to 30/04/2017. The study was done after obtaining clearance from the Institutional Human Ethics Committee and written informed consent from the patients.

Sample size is calculated using duration of analgesia as the primary outcome based on previous studies.

$N = 2x(z\alpha+z\beta)^2 \times SD^2 / (M_c - M_t)^2$

SD=510mts $Z\alpha$=5%(1.96)

Mc =1428 mts $Z\beta$=80%(0.84)

M_t=1044 mts

$n = 2x\ 7.84x\ 510x\ 510\ /(1428-1044)^2 = 27.66$

Hence 28 patients in each group.

We planned 30 patients in each group

INCLUSION CRITERIA:

- Patient acceptance
- ASA 1 & 2 patients
- Patients aged between 20-70 years
- All patients posted for elective upper limb surgeries under Supraclavicular Brachial Plexus block

EXCLUSION CRITERIA:

- Patients with history of allergy to local anaesthetics
- Patients on steroid therapy
- Patient with Diabetes and Coagulopathies
- Infection at the site of proposed puncture for block
- Neuropathies

Routine pre-operative assessment of the patients was done on the previous day of surgery. The patients were pre-medicated with tablet Ranitidine 150 mg on the night before surgery and on the day of surgery. Starvation guidelines were followed. The patients were randomly allocated into two groups (group 1 and group 2).

After shifting the patient to the operating room ASA standard monitors ECG, blood pressure, and oxygen saturation were connected and recorded. Intravenous line was secured.

The consultant in the operating room who was not involved in the study prepared the study drug according to the random groups. All vital parameters were recorded every 5 minutes. Under aseptic precautions supraclavicular Brachial plexus block was performed using a nerve stimulator.

Group 1: Patients received 3mg/kg of Bupivacaine and 8 mg(2ml) ofDexamethasone perineurally and 2ml normal saline intravenously.

Group 2: Patients received 3mg/kg of Bupivacaine and 2 ml of normal saline perineurally and 8mg (2ml) of Dexamethasone intravenously.

The time of injection of the local anaesthetic, onset of complete sensory and motor blockade was noted and recorded. Patients were followed up post-operatively and the time of administration of first analgesic was recorded. The severity of pain at the time of administration of analgesic was graded with the verbal analogue scale.

DEFINITIONS:

Onset of sensory blockade is defined as the time interval between the end of local anaesthetic administration to loss of sensation to needle prick.In our study this was tested using needle prick method .

Onset of motor blockade is defined as the time interval between the end of administration of the local anaesthetic to inability to move the fingers. In our study it was tested using the modified Bromage score.

Duration of sensory blockade is defined as the time interval between the completion of injection of local anaesthetic to the administration of first analgesic to the patient.

TABLE 3 : MODIFIED BROMAGE SCALE:

GRADE 0	Normal motor function with flexion/ extension of elbow wrist and fingers
GRADE 1	Decreased motor function with ability to move fingers or wrist only
GRADE 2	Complete motor blockade with inability to move fingers

Table 4 : VERBAL ANALOGUE SCALE:

TYPE OF PAIN	**SCORE**
No pain	0
Mild pain	1
Moderate pain	2
Severe pain	3

STATISTICAL ANALYSIS

All data were entered in Microsoft excel 2010 and statistical analysis was performed using the software SPSS version 23.0. Data was expressed as percentages and mean values with standard deviations. Differences between both the groups were analysed using the independent sample ‘t’ test and the Pearson’s chi square test. Results were defined as statistically significant if the ‘p’ value was less than 0.05.

RESULTS AND OBSERVATION

TABLE 5 : AGE DISTRIBUTION BETWEEN TWO GROUPS

AGE IN YEARS	GROUP 1		GROUP 2	
	No. of Patients	Percentage	No. of patients	Percentage
30 and below	5	16.6	9	30
31-40	5	16.6	3	10
41-50	9	30	8	26.6
51-60	7	23.3	7	23.3
61-70	3	10	1	3.3
>70	1	3.3	2	6.6
TOTAL	30	100	30	100
Mean ± SD	45.7± 7.87		43 ± 9.07	
'p' VALUE	0.685			

According to the above table, the mean age in group 1 was found to be 45.7 and that in group 2 was 43. The 'p' value was found to be 0.685. Hence there is no significant statistical difference between the age distribution in both the groups.

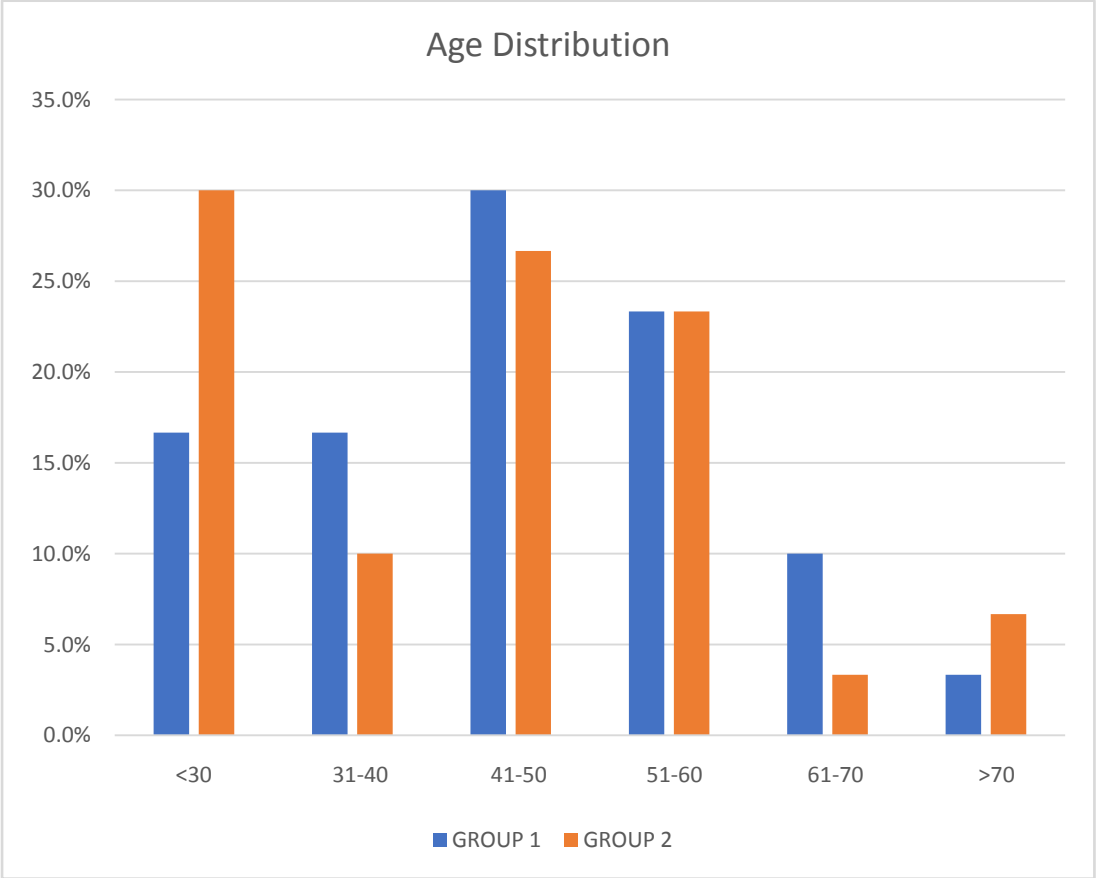


FIGURE 16 : AGE DISTRIBUTION IN BOTH GROUPS

TABLE 6: GENDER DISTRIBUTION BETWEEN TWO GROUPS

GENDER	GROUP 1		GROUP 2	
	No. of patients	Percentage	No. of patients	Percentage
MALE	19	63.33	20	67.3
FEMALE	11	36.66	10	33.3
TOTAL	30	100	30	100
'p' VALUE	0.861			

There was no significant statistical difference of gender distribution between group 1 and 2 according to the 'p' value of 0.861.

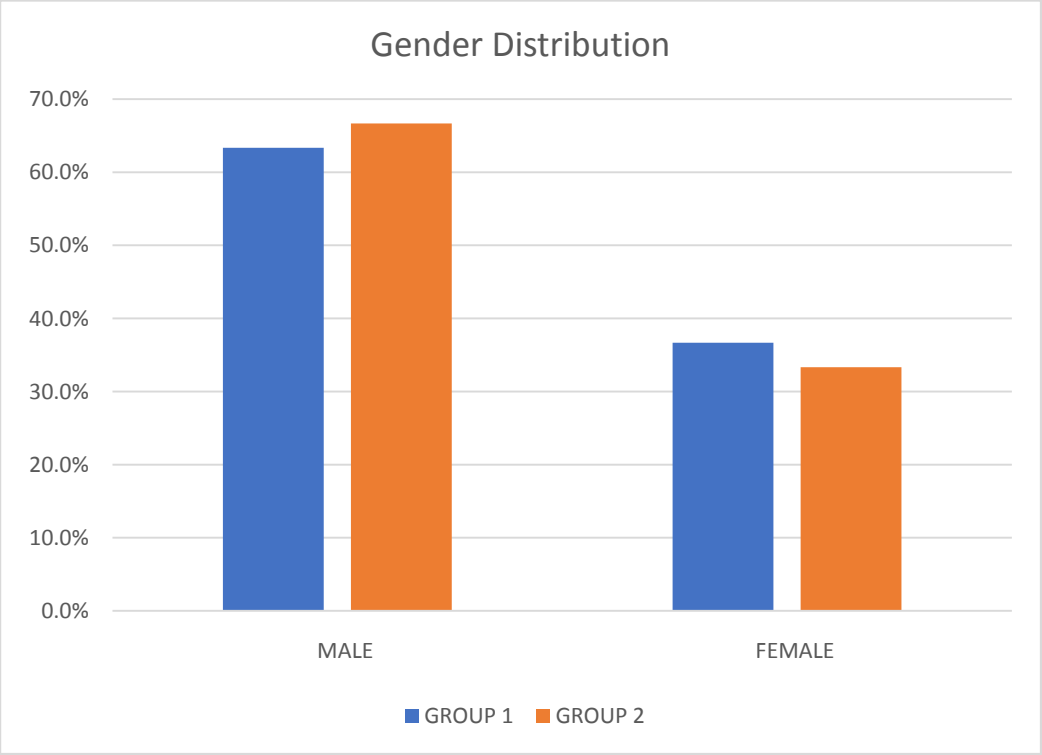


FIGURE 17 : GENDER DISTRIBUTION BETWEEN TWO GROUPS

TABLE7 :WEIGHT DISTRIBUTION BETWEEN TWO GROUPS

AGE IN YEARS	GROUP 1		GROUP 2	
	No. of Patients	Percentage	No. of patients	Percentage
50 & below	8	26.7	4	13.3
51-60	11	36.7	13	43.3
61-70	6	20.0	8	26.7
>70	5	16.7	5	16.7
TOTAL	30	100	30	100
Mean ± SD	58.4		62.5	
'p' VALUE	0.240			

Weight distribution between the two groups were calculated and the mean weight was found to be 58.4 in group 1 and 62.5 in group 2. The weight distribution in both the groups did not show any significant statistical difference according to the 'p' value of 0.240.

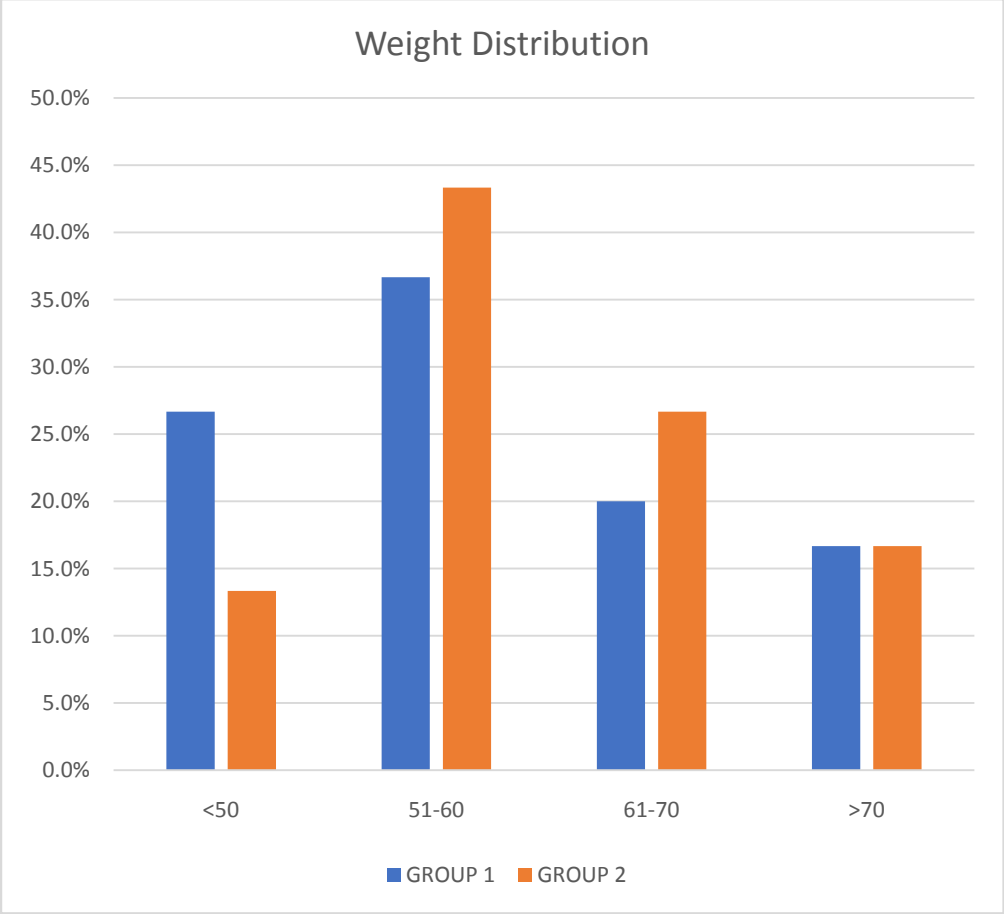


FIGURE 18: WEIGHT DISTRIBUTION BETWEEN TWO GROUPS

TABLE 8: ONSET OF SENSORY BLOCKADE IN GROUP 1

Sensory onset	No. of Patients	Percentage
Onset < 14 minutes	10	33.33
Onset > 15 minutes	20	66.66
Total	30	100
Mean ± SD	15.23± 2.60	

For statistical purpose, the onset of sensory blockade was segmented into two categories according to the mean and median values. According to the statistical analysis mean sensory onset in both groups was 14.47 with a median value of 15. Hence the grouping was done as sensory onset less than 14 minutes and more than 15 minutes.

In group 1, 33% of patients had a sensory onset below 14 minutes and 66% of patients had sensory onset more than 15 minutes. The mean sensory onset in group 1 was found to be 15.23.

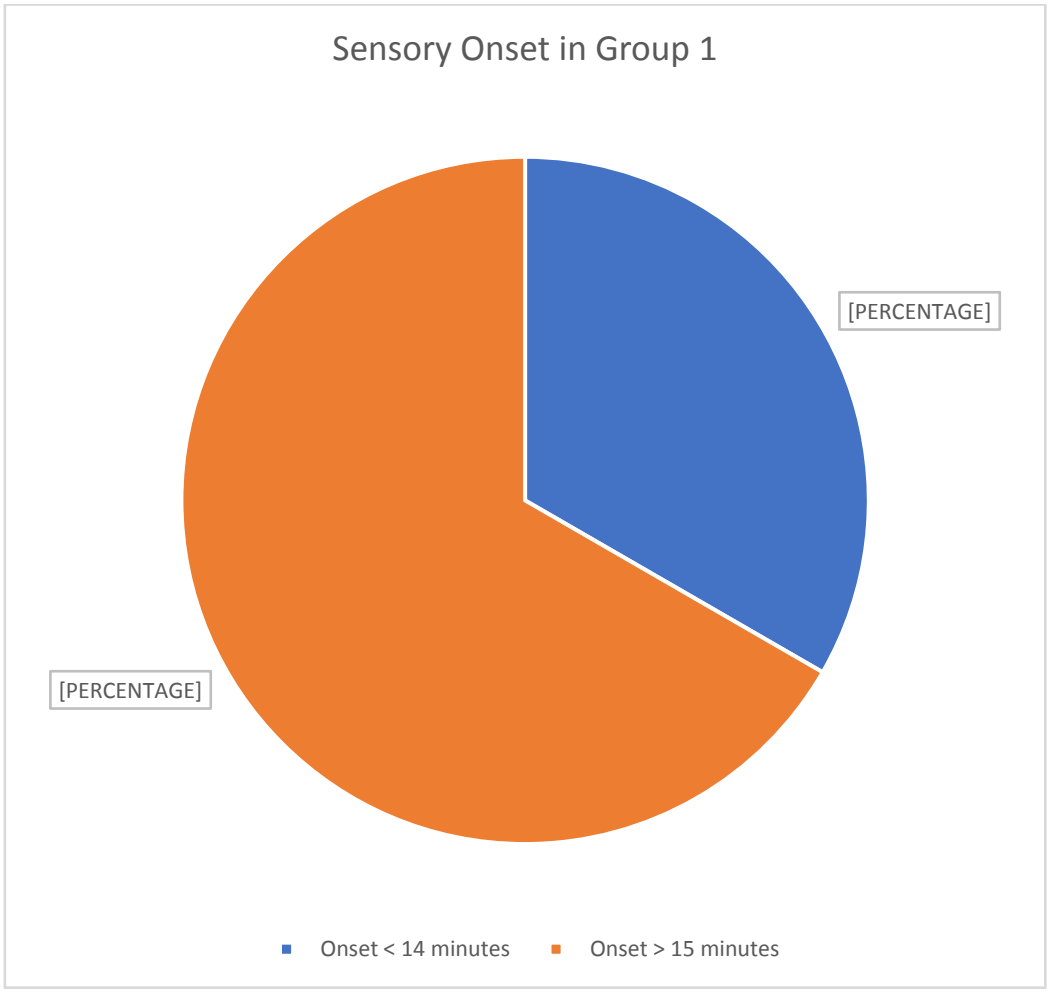


FIGURE 19: ONSET OF SENSORY BLOCKADE IN GROUP 1

TABLE 9: ONSET OF SENSORY BLOCKADE IN GROUP 2

Sensory Onset	No. of Patients	Percentage
Onset < 14 minutes	11	36.7
Onset > 15 minutes	19	63.3
Total	30	100
Mean ± SD	14.45± 1.97	

In group 2, 36.6 % of patients had sensory onset less than 14 minutes and 63.3%of patients had a sensory onset of more than 15 minutes. The mean sensory onset in group 2 was found to be 14.45.

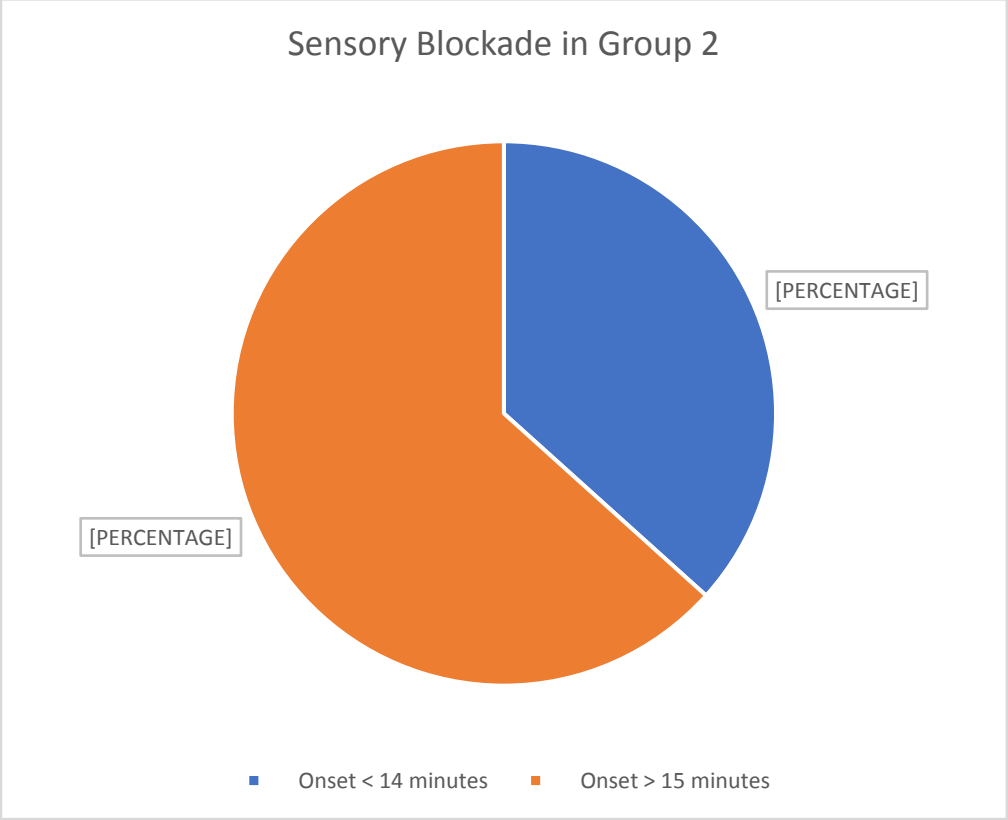


FIGURE 20: SENSORY ONSET IN GROUP 2

TABLE 10: COMPARISON OF SENSORY ONSET IN BOTH GROUPS

SENSORY ONSET	Group 1		Group 2	
	No of Patients	Percentage	No of Patients	Percentage
Onset < 14 mts	10	33.33	11	36.7
Onset > 15 mts	20	66.66	19	63.3
Total	30	100	30	100
Mean ± SD	15.23±2.60		14.45±1.97	
p value	0.861			

When the sensory onset in both the groups were compared, there was no significant statistical difference according to the 'p' value of 0.861.

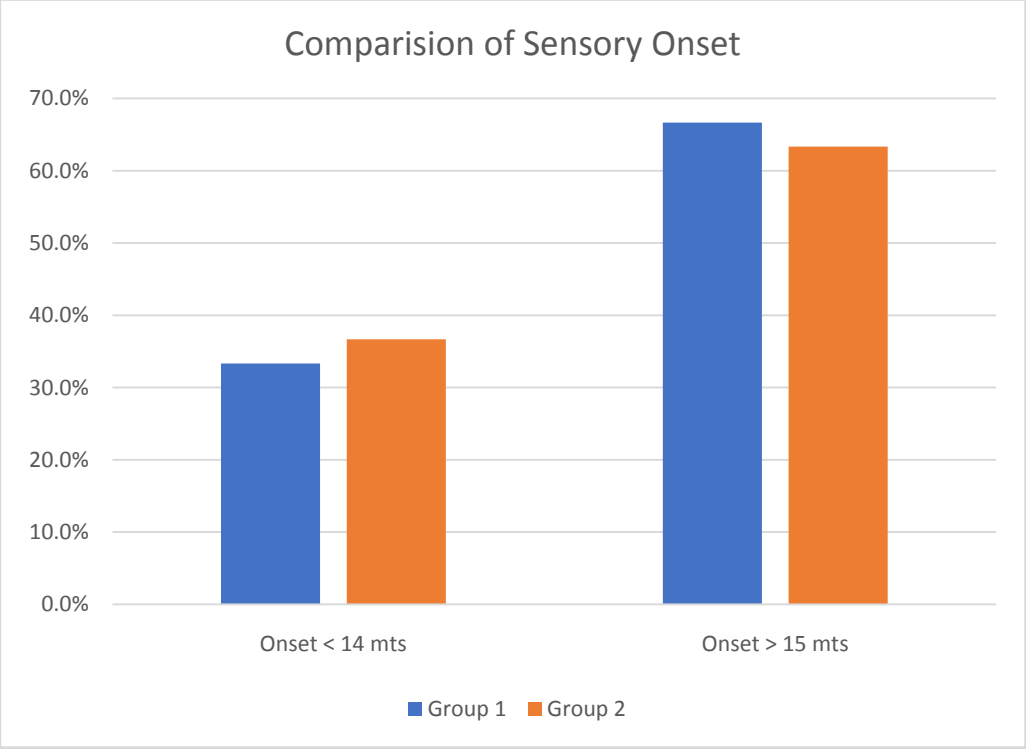


FIGURE 21: COMPARISON OF SENSORY ONSET IN BOTH GROUPS

TABLE 11: ONSET OF MOTOR BLOCKADE IN GROUP 1

Motor onset	No. of patients	Percentage
Onset < 17 minutes	17	56.67
Onset > 18 minutes	13	43.33
Total	30	100
Mean ± SD	17.21±2.09	

For statistical purpose, the onset of motor blockade was segmented into two categories according to the mean and median values. According to the statistical analysis mean sensory onset in both groups was 17.14 with a median value of 17. Hence the grouping was done as motor onset less than 17 minutes and more than 18 minutes.

In group 1, 58.62% of patients had a motor onset of less than 17 minutes and 43.33% had a motor onset of more than 18 minutes. The mean motor onset in group 1 was found to be 17.21.

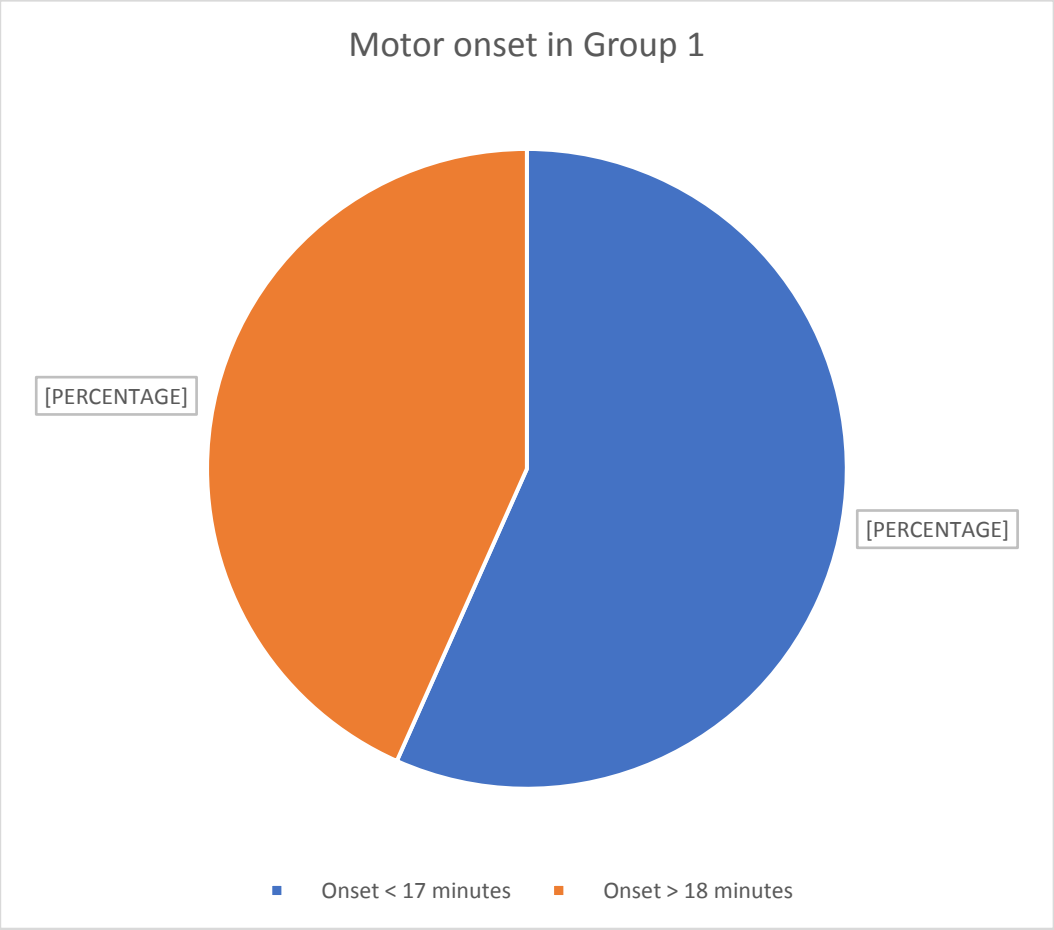


FIGURE 22: MOTOR ONSET IN GROUP 1

TABLE 12: ONSETOF MOTOR BLOCKADE IN GROUP 2

Motor onset	No. of patients	Percentage
Onset < 17 minutes	13	43.33
Onset > 18 minutes	17	56.67
Total	30	100
Mean ± SD	17.34±2.39	

In group 2, 48.3% of patients had a motor onset of less than 17 minutes and 56.6% of patients had a motor onset of more than 18 minutes.

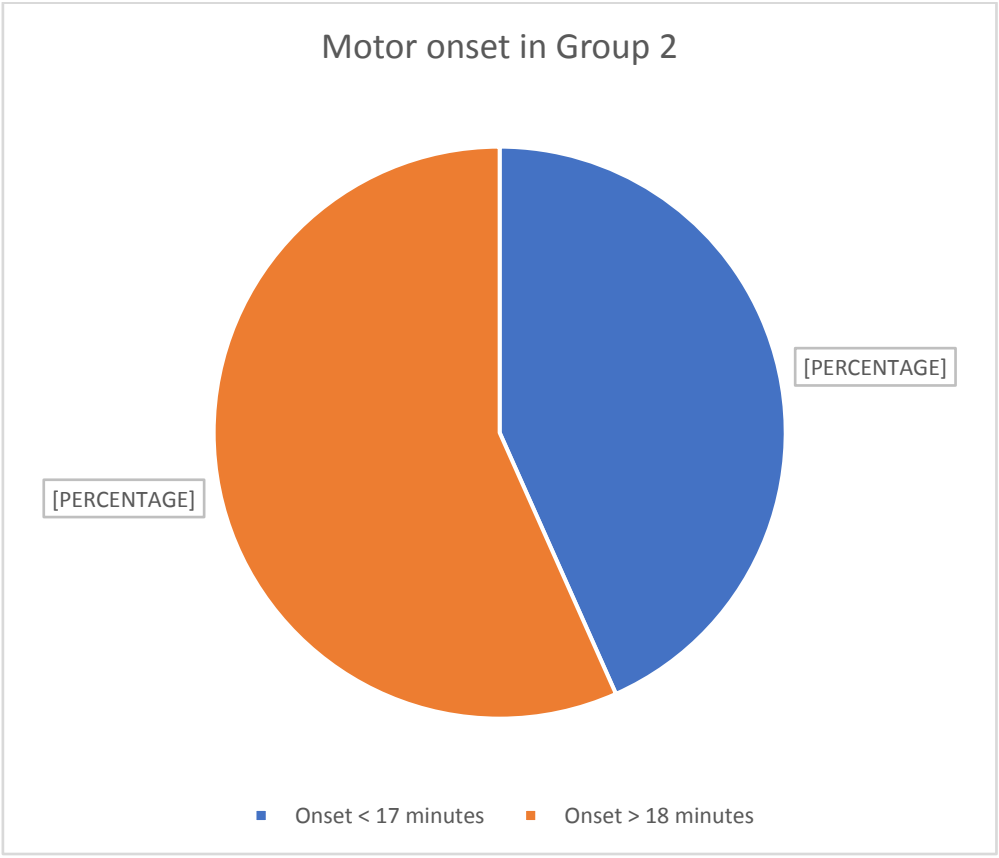


FIGURE 23: MOTOR ONSET IN GROUP 2

TABLE 13: COMPARISON OF MOTOR ONSET IN BOTH GROUPS

MOTOR ONSET	Group A		Group B	
	No of Patients	Percentage	No of Patients	Percentage
Motor Onset< 17 mts	17	56.66	13	43.33
Motor Onset > 18mts	13	43.33	17	56.67
Total	30	100	30	100
Mean± SD	17.21±2.09		17.34±2.390	
p value	0.240			

The mean motor onset was 17.21 in group 1 and 17.34 in group 2. According to the 'p' value of 0.240 there was no significant statistical difference in onset of motor blockade between both the groups.

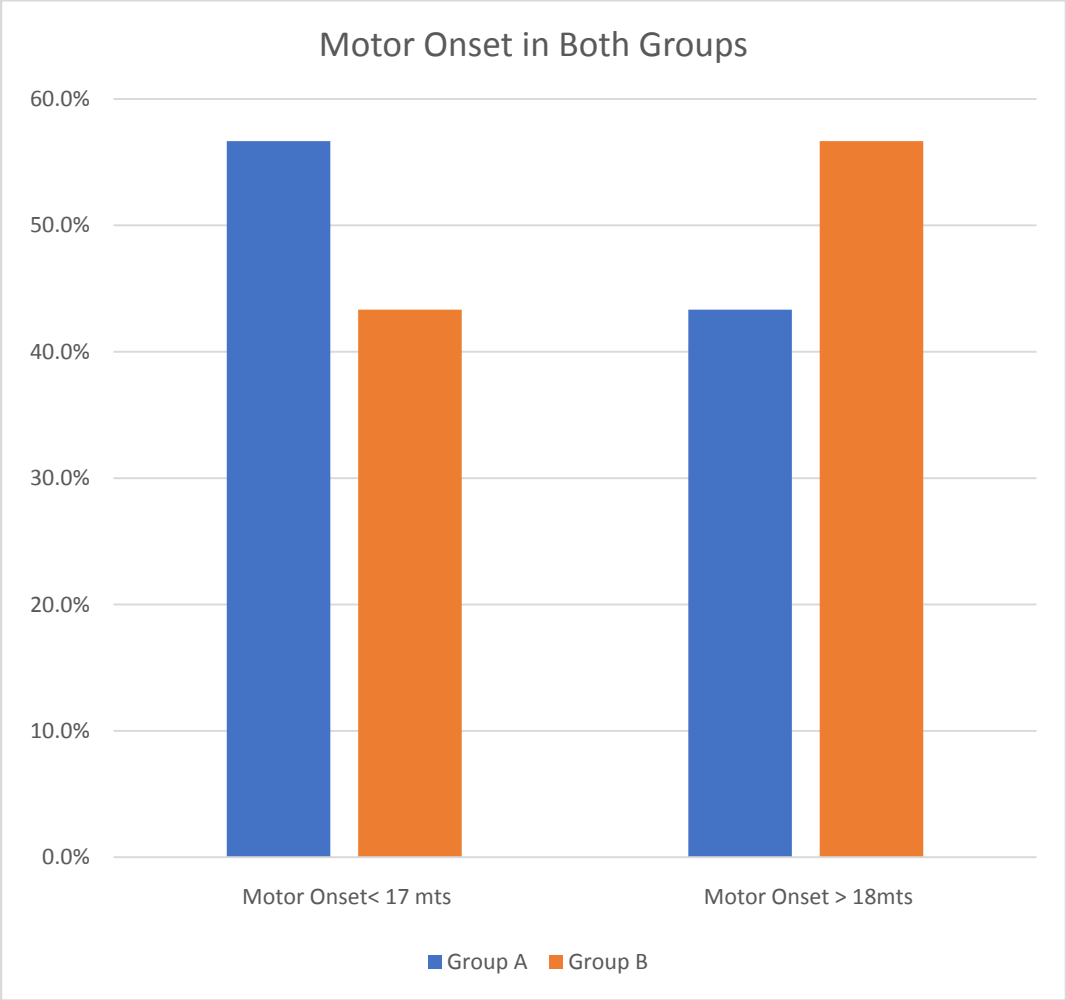


FIGURE 24: COMPARISON OF MOTOR ONSET IN BOTH GROUPS

TABLE 14: DURATION OF ANALGESIA IN GROUP 1

Duration of analgesia	No. of Patients	Percentage
Analgesia< 36 hours	11	36.66
Analgesia> 37 hours	19	63.33
Total	30	100
Mean ± SD	38.89±3.31	

Duration of analgesia was segmented into two, based on the mean and median values. According to statistical analysis the mean duration of analgesia ws found to be 35 hrs and the median was found to be 36 hrs.

In group 1, 36.6 % of patients had a analgesic duration of less than 36hours and 63.3 % of patients had analgesia for more than 37 hours. The mean analgesic duration in group 1 was found to be 38.89.

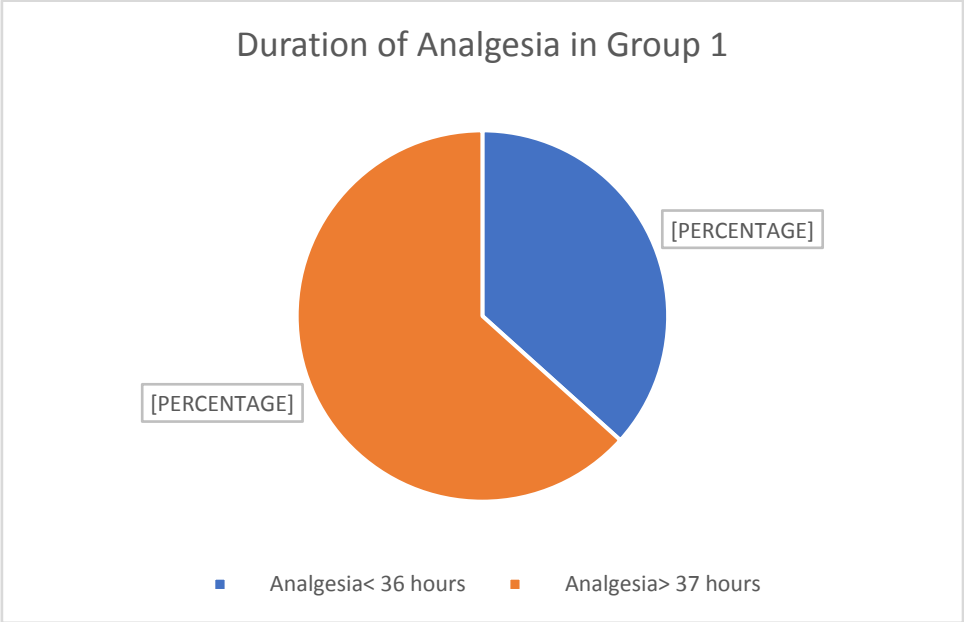


FIGURE 25 : DURATION OF ANALGESIA IN GROUP 1

TABLE 15: DURATION OF ANALGESIA IN GROUP 2

Duration of analgesia	No. of Patients	Percentage
Analgesia < 36 hours	18	60
Analgesia > 37 hours	12	40
Total	30	100
Mean±SD	34.39±2.78	

In group 2, 60% of patients had analgesia duration of less than 36 hours and 40% of patients had analgesia more than 37 hours. The mean analgesia duration in group 2 was found to be 34.39.

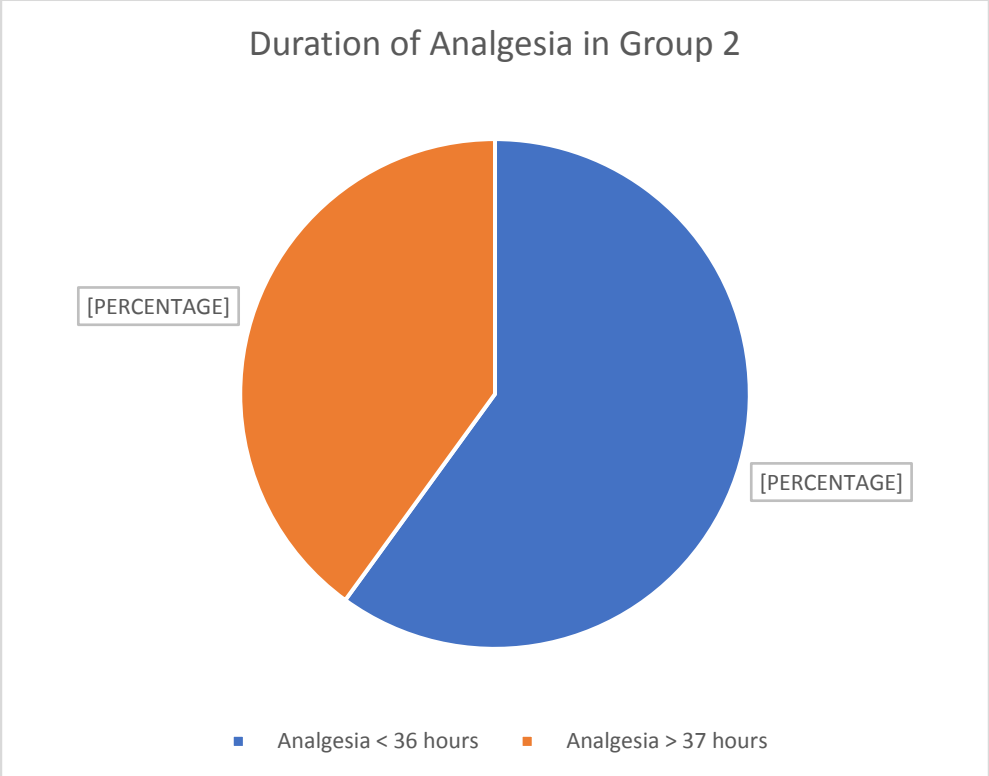


FIGURE 26: DURATION OF ANALGESIA IN GROUP 2

TABLE 16 : COMPARISON OF DURATION OF ANALGESIA IN BOTH GROUPS

ANALGESIA DURATION	Group 1		Group 2	
	No of Patients	Percentage	No of Patients	Percentage
Duration < 36 hrs	11	36.66	18	60
Duration> 37 hrs	19	63.33	12	40
Total	30	100	30	100
Mean± SD	38.89±3.31		34.39±2.78	
p value	0.240			

When duration of analgesia was compared between the two groups, there was no significant statistical difference according to the ‘p’ value of 0.240.

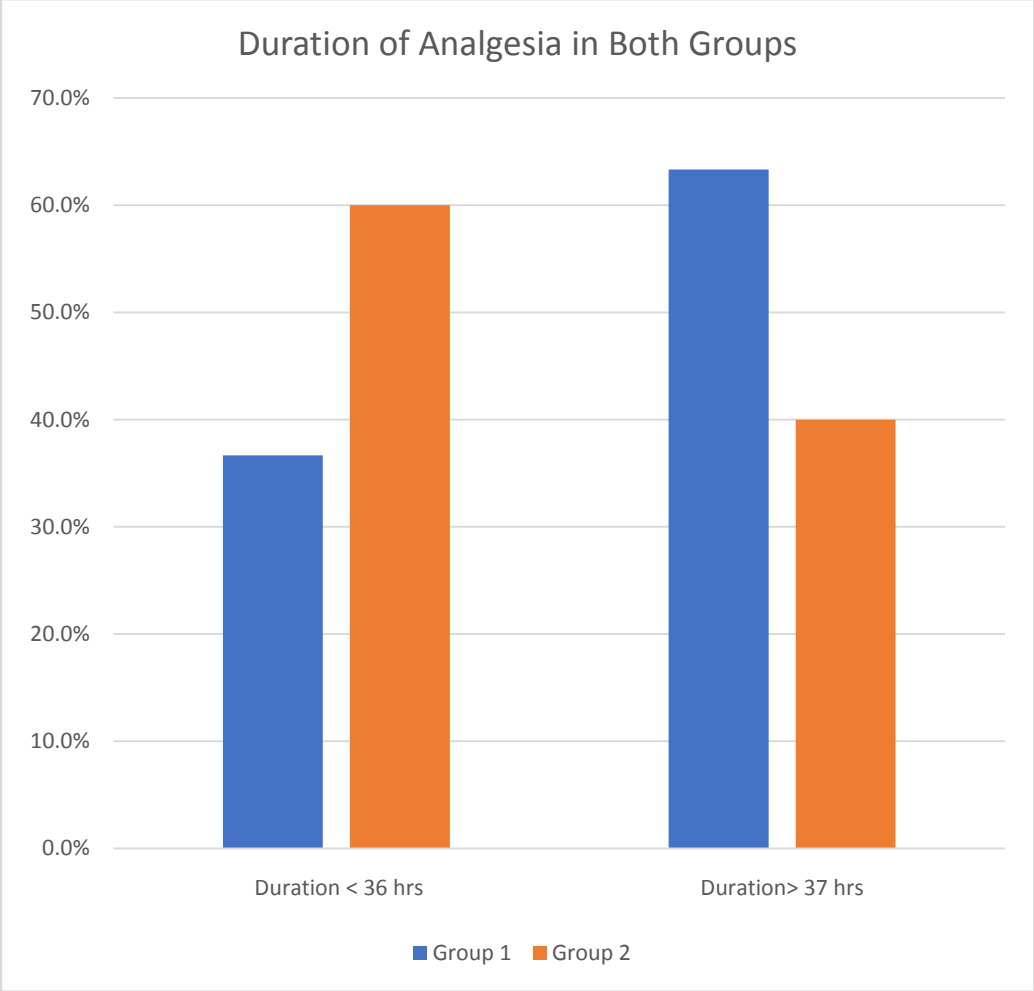


FIGURE 27: COMPARISON OF DURATION OF ANALGESIA IN BOTH GROUPS

DISCUSSION

Post- operative pain is the commonest complaint in patients undergoing upper limb surgeries. Administration of multiple analgesics in the post-operative period often may result in a number of adverse effects. Brachial plexus block is a simple, safe and effective technique which provides adequate analgesia. It also avoids the complications of general anaesthesia[2]. Single shot nerve blocks often fail to provide extended analgesia in the post-operative period, hence the use of additives with local anaesthetics to prolong the duration of sensory blockade is practiced[41].

Many additives have been used with local anaesthetics to prolong analgesic duration and also to improve the quality of the regional block[6,12]. The addition of glucocorticoids with local anaesthetics in brachial plexus supraclavicular blocks significantly prolongs analgesia without much side effects[42,43]. The analgesic effect of Dexamethasone added to local anaesthetics in the perineural route has been studied and proved in the recent past. The mechanism of action of locally administered Dexamethasone is probably by increasing the activity of inhibitory potassium channels on nociceptive 'C' fibres. It also causes some amount of vasoconstrictor effect[27,28].

The route of administration of Dexamethasone for prolonged analgesia in Brachial plexus Supraclavicular block remains a controversy. It is shown that perineural Dexamethasone may cause potential neurotoxicity but is not proved and evidences are also inconclusive[12].

The use of IV Dexamethasone for prolonged post-operative analgesia is being studied recently. Analgesic effect of systemically administered Dexamethasone could be due to decreased production of inflammatory mediators and increased production of anti-inflammatory mediators as a result of binding of cytoplasmic glucocorticoid receptors to glucocorticoid response elements in the DNA[12,13].

Very few studies have been done comparing the analgesic effect of Dexamethasone administered IV or perineurally in Brachial Plexus block. In our study we have compared the duration of analgesia with 8 milligram of Dexamethasone administered IV and perineurally in 60 patients undergoing elective upper limb surgeries under supraclavicular Brachial plexus block.

In our study the demographic variables like, age, gender and weight were comparable between both the groups and no significant difference occurred between them in both the groups.

ONSET OF SENSORY BLOCKADE:

The onset of sensory blockade was comparable between both the groups. The mean sensory onset in group 1 was found to be 15.23 minutes and that in group 2 was 14.45 minutes. Though the mean sensory onset in group 2 was lower than that in group 1 the difference was not statistically significant according to the ‘p’ value.

Our results matched with the results of the study done by Parveen et al [2] in 2015 who also inferred that no significant statistical difference occurred

between the onset of sensory blockade in the IV and the perineural group. The studies conducted by Desmet et al[1] and Rosenfeld et al[12] also did not show any significant difference in the onset of sensory blockade between the perineural and the IV groups.

ONSET OF MOTOR BLOCKADE:

The onset of motor block was compared in both the groups. The mean motor onset in group 1 was found to be 17.21 minutes and the mean motor onset in group 2 was 17.34 minutes. There was no major difference in the motor onset of both the groups and hence it was not statistically significant.

In a study conducted by Allarasan et al[44] to compare the effects of perineural Dexamethasone in supraclavicular block, they had a significant difference between the onset of motor blockade in the control group and the Dexamethasone group. Dexamethasone group had a shorter onset of motor blockade compared with the other group. In a study conducted by Abdallah et al[13] for comparing effects of IV and perineural Dexamethasone in supraclavicular brachial plexus block, the time of motor onset was lesser in the IV and the perineural group than the control group but no statistically significant difference was present in the onset of motor blockade between the IV and the perineural groups. Our results on onset of motor blockade also were consistent with the result of the study conducted by Abdallah et al.

DURATION OF ANALGESIA:

The mean duration of analgesia in group 1 was found to be 38.89 hours and that in group 2 was found to be 34.39 hours. Though the mean analgesia duration in group 2 was lower than the mean analgesia duration in group 1 there was no significant statistical difference in the analgesia duration between the two groups.

Our study results matched with the results of the study conducted by Abdallah et al who also inferred that both IV and perineural Dexamethasone similarly prolonged duration of analgesia in Supraclavicular brachial plexus block. In another study conducted by Kawanishi et al[45] in comparing the effects of Dexamethasone 4mg with interscalene brachial plexus block using Ropivacaine, they concluded that only perineural Dexamethasone prolonged analgesia duration as compared to the control group.

SUMMARY

A study titled “Comparison of IV and perineural Dexamethasone in prolonging duration of analgesia in Supraclavicular Brachial plexus block” was carried out in PSG Institute of Medical Sciences and Research during the period 01/07/2016 to 30/04/2017.

The study included 60 patients randomly divided into two groups of 30 patients in each group. One group received Dexamethasone 8 mg perineurally with supraclavicular block and the other group received Dexamethasone 8mg IV along with supraclavicular block. Parameters such as onset of sensory and motor blockade and duration of analgesia was noted.

All data were entered in Microsoft excel 2010 and were analysed in SPSS software version 23.0. Demographic variables such as age, gender and weight were comparable between both the groups and no significant difference existed between both the groups. The onset of sensory and motor blockade was similar in both the groups and showed no significant statistical difference.

The primary outcome of the study was duration of analgesia. The mean duration of analgesia was less in the IV group as compared with the perineural group but the results were not statistically significant.

CONCLUSION

Both IV and perineural Dexamethasone similarly prolonged the duration of analgesia in Supraclavicular Brachial Plexus block. The onset of sensory and motor blockade showed no difference between the two groups. The mean duration of analgesia in the perineural group was slightly higher as compared to the IV group but the results were not statistically significant. Due to the existence of some controversies over perineural use of Dexamethasone, IV Dexamethasone can be used as a safer alternative to prolong duration of analgesia in patients undergoing upper limb surgeries under Supraclavicular Brachial plexus block.

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Study Volunteer ID:
Study Volunteer Name:

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I / We (write name of the investigator(s) here), Dr. J.Keerthana, am / are carrying out a study on the topic: " Comparison of perineural and Intravenous Dexamethasone in duration of analgesia in Supraclavicular Brachial plexus block" as part of my / our research project being carried out under the aegis of the Department of:

(*Applicable to students only*): My / our research guide is: Dr.S.Mushahida

The justification for this study is: i.) Dexamethasone as an adjuvant to local anaesthetics in brachial plexus block is proven to prolong duration of analgesia
ii.) Use of systemic Dexamethasone to prolong analgesia is recently being studied
iii.) Hence we will be comparing two routes (perineural and IV) Dexamethasone for prolonging duration of anaesthesia

The objectives of this study are:

Primary Objective: To compare the effects of perineural and IV Dexamethsone on duration of analgesia in in adult patients posted for upper limb surgeries under Supraclavicular Brachial Plexus block

Sample size: 60.

Study volunteers / participants are (specify population group & age group): patients aged 20-70 years .

Location: PSGIMSR.

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study.

Data collected will be stored for period of 3 years. We will not use the data as part of another study

Medication given, if any, duration, side effects, purpose, benefits: Dexamethasone will be given in Perineural and Intravenous route.
Dexamethasone prolongs the duration of analgesia post operatively

Whether medication given is part of routine procedure**:** **NO** (If not, state reasons for giving this medication)
Dexamethasone has prolonged analgesia with minimum side effects

Whether alternatives are available for medication given: **Yes** (If yes, state reasons for giving this particular medication) because other drugs have many side effects

Benefits from this study: Helps to choose a better route of drug administration for prolonging post operative analgesia

Risks involved by participating in this study: No risks

How the **results** will be used:

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: 8870877244

Contact number of Ethics Committee Office: During Office hours: 0422 2570170 Extn.: 5818
After Office hours: 9865561463

PATIENT PROFORMA

Serial No:

Name: Age/sex:

OP No: IP No: Ht: Wt: BMI:

Diagnosis:

Procedure:

Baseline vitals:

BP: HR: $Spo_{2:}$

PARAMETER	DATE&TIME	DURATION
Completion of injection of local anaesthetic		
Onset of sensory blockade		
Onset of motor blockade		
Administration of first analgesic post-operatively		

VERBAL RATING SCORE

TYPE OF PAIN	SCORE
No pain	1
Mild pain	2
Moderate pain	3
Severe pain	4

பூ சா கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை

மனித நெறிமுறைக் குழு

ஒப்புதல் படிவம்

தேதி :

ஜெ. கீர்த்தனா ஆகிய நான், பூ சா கோ மருத்துவக் கல்லூரியின் / மருத்துவ மனையின் மயக்கவியல் துறையின் கீழ், **புயநரம்பு பின்னல் பிளாக்கின் போது வலி நிவாரண நேரம் நீட்டிக்க டெக்ஸாமெத்தசோன் நாளம் மற்றும் நரம்பை சுற்றி செலுத்துவதில் எது சிறந்தது என்று ஒப்பிடுதல்** என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி (மாணவர்களுக்கு மட்டும்): **மரு.S. முஷைதா,**

பேராசிரியை மற்றும் துறைத்தலைவர்,

மயக்கவியல் துறை,

பூ சா கோ மருத்துவக் கல்லூரி.

ஆய்வு மேற்கொள்வதன் அடிப்படை :

புயநரம்பு பின்னல் பிளாக்கில் வலியின்மையை நீட்டிக்க நிறைய மருந்துகள் கொடுக்கப்படுகின்றன. நாளம் மூலம் டெக்ஸமெத்தசோன் கொடுத்து வலிநீட்டிக்கும் முறை தற்பொழுது ஆராயப்பட்டு வருகிறது. எனவே இந்த ஆராய்ச்சியை மேற்கொள்கிறேன். இந்த ஆய்வில் புயநரம்பு பின்னல் நரம்பினை மரத்துப்போக செய்யும் பிளாக்கின் போது இந்த மருந்தினை நாளத்தில் கொடுத்தும், மயக்கமருந்துகளுடன் நரம்பை சுற்றி கொடுத்தும் வலியின்மையை அதிக நேரம் நீட்டிக்க எது உதவும் என்று ஒப்பிட்டு பார்க்கப்படும்.

ஆய்வின் நோக்கம் :

1. கைகளில் அறுவை சிகிச்சை செய்யும் முன் கொடுக்கப்படும் சுப்ராகிளாவிக்குளர் புயநரம்பு பின்னல் பிளாக்கில் வலியின்மையை அதிக நேரம் நீட்டிப்பதற்கு டெக்சாமெத்தசோன் நாளம் அல்லது நரம்பை சுற்றி கொடுப்பது ஆகிய இரண்டு வழிகளில் எது சிறந்தது என்று ஒப்பிட்டு பார்ப்பது.
2. அறுவை சிகிச்சைக்குப்பின் வலியின்மைக்கு கொடுக்கப்படும் மருந்துகளை குறைப்பது.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை : 60

ஆய்வில் பங்கு பெறுவோர் மற்றும் வயது : 20 – 70 வயதுக்குட்பட்ட ஆண்கள் மற்றும் பெண்கள்

ஆய்வு மேற்கொள்ளும் இடம் : பூ சா கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை

இந்த ஆய்வில் எங்களுடன் ஒத்துழைக்குமாறு கேட்டுக்கொள்கிறோம். நாங்கள் சில தகவல்களை இந்த ஆய்விற்காக சேகரிக்க உள்ளோம்.

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் 3 வருடங்கள் பாதுகாக்கப்படும். இந்தத் தகவல்கள் வேறு ஆய்விற்குப் பயன்படுத்தப்பட மாட்டாது.

மருந்துகள் ஏதேனும் கொடுக்கப் பட்டிருந்தால் அவை பற்றிய விவரம் :

டெக்ஸாமெத்தசோன் நாளங்களில் மற்றும் நரம்புகளைசுற்றி வலியின்மை நீட்டிக்க கொடுக்கப்படுகிறது.

மருந்துகள் கொடுக்கப்படுவது வழக்கமான சிகிச்சை முறையா? இல்லை

டெக்ஸாமெத்தசோன் வலியின்மையை குறைவான பக்கவிளைவுகளுடன் அதிக நேரம் நீட்டிக்க செய்கிறது.

கொடுக்கப்பட்ட மருந்துகளுக்கு மாற்று உள்ளதா ?: ஆம்

மற்ற மருந்துகளில் பக்கவிளைவுகள் அதிகம்.

ஆய்வில் பங்கு பெறுவதால் ஏற்படும் பலன்கள் :

அறுவை சிகிச்சைக்குப்பின் வலியின்மை நீட்டிக்க எந்த வழி சிறந்தது என்ற தேர்ந்து எடுத்தல்.

ஆய்வில் பங்கேற்பதால் ஏற்படும் அசௌகரியங்கள் / பக்க விளைவுகள் : ஏதும் இல்லை

ஆய்வின் முடிவுகள் எந்த முறையில் பயன்படுத்தப்படும்?

புயநரம்பு பின்னல் பிளாக்கின்போது வலியின்மையை அதிக நேரம் நீட்டிக்க சிறந்த வழியில் டெக்சாமெத்தசோன் கொடுக்கப்படும். இதனால் வலி நிவாரண மருந்துகளின அளவு குறைக்கப்படும்.

இந்த ஆய்வின் கேள்விகளுக்கு பதிலளிப்பதிலோ, இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் எடுப்பதிலோ உங்களுக்கு ஏதேனும் அசௌகரியங்கள் இருந்தால், எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உண்டு. எப்பொழுது வேண்டுமானாலும் ஆய்விலிருந்து விலகும் உரிமை உங்களுக்கு உள்ளது. ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சை முறையில் எந்த வித பாதிப்பும் இருக்காது என்று உங்களுக்கு உறுதியளிக்கிறோம். மருத்துவ முறையில் நோயாளிகளுக்கு அளிக்கப்படும் சேவைகளை நீங்கள் தொடர்ந்து பெறலாம். இந்த ஆய்வில் பங்கேற்க ஒப்புகொள்ளுவதால் வேறு எந்த விதமான கூடுதலான பலனும் உங்களுக்கு கிடைக்காது. நீங்கள் அளிக்கும் தகவல்கள் இரகசியமாக வைக்கப்படும். ஆய்வில பங்கேற்பவர்கள் பற்றியோ அவர்கள் குடும்பத்தைப் பற்றியோ எந்தத் தகவலும் எக்காரணம் கொண்டும் வெளியிடப்படாது என்று உறுதியளிக்கிறோம். நீங்கள் அளிக்கும் தகவல்கள் / இரத்தமாதிரிகள் / திசு மாதிரிகள் அங்கீகரிக்கப்பட்ட ஆய்விற்கு மட்டுமே பயன்படுத்தப்படும். இந்த ஆய்வு நடைபெறும் காலத்தில குறிப்பிடத்தகுந்த புதிய

கண்டுபிடிப்புகள் அல்லது பக்க விளைவுகள் ஏதும் ஏற்பட்டால் உங்களுக்குத் தெரிவிக்கப்படும். இதனால் ஆய்வில் தொடர்ந்து பங்கு பெறுவது பற்றிய உங்கள் நிலைப்பாட்டை நீங்கள் தெரிவிக்க ஏதுவாகும்.

ஆய்வுக்குட்படுபவரின் ஒப்புதல் : இந்த ஆய்வைப் பற்றிய மேற்கூறிய தகவல்களை நான் படித்து அறிந்து கொண்டேன் / ஆய்வாளர் படிக்கக் கேட்டுத் தெரிந்து கொண்டேன். ஆய்வினைப் பற்றி நன்றாகப் புரிந்து கொண்டு இந்த ஆய்வில் பங்கு பெற ஒப்புகொள்கிறேன். இந்த ஆய்வில் பங்கேற்பதற்கான எனது ஒப்புதலை கீழே கையொப்பமிட்டு / கைரேகை பதித்து நான் தெரிவித்துக்கொள்கிறேன்.

பங்கேற்பாளரின் பெயர் , முகவரி :

பங்கேற்பாளரின் கையொப்பம் / கைரேகை / சட்டபூர்வ பிரதிநிதியின் கையொப்பம் :

தேதி :

ஆய்வாளரின் கையொப்பம் :

தேதி

ஆய்வாளரின் தொலைபேசி எண் : 8870877244

மனிதநெறிமுறைக் குழு அலுவலகத்தின் தொலைபேசி எண்:

அலுவலக நேரத்தில் : 0422 2570170 5818

அலுவலக நேரத்திற்குப்பின் : 9865561463

S.No	AGE	GENDER	WEIGHT	GROUP	Sensory onset	Motor onset	Analgesia Duration
1	58	2	59	1	12	15	35 hours
2	43	1	75	1	15	17	32 hours
3	40	1	64	2	8	13	37 hours
4	61	2	45	1	15	18	38 hours
5	53	2	58	2	10	12	36 hours
6	60	1	65	2	12	15	34 hours
7	22	1	80	2	15	18	32 hours
8	44	2	68	2	10	14	31 hours
9	34	1	78	1	14	15	38 hours
10	37	1	50	2	14	14	32 hours
11	65	1	70	1	13	15	38 hours
12	47	1	72	2	15	17	32 hours
13	45	1	48	1	17	18	38 hours
14	42	1	60	1	15	18	36 hours
15	42	1	60	2	12	18	28 hours
16	48	1	72	2	10	14	28 hours
17	24	1	58	1	7	12	32 hours
18	29	2	50	2	8	15	32 hours
19	42	1	70	1	12	17	37 hours
20	60	2	55	1	15	18	38hours
21	26	1	80	2	18	22	28 hours
22	46	2	45	1	13	17	40 hours
23	73	2	50	2	17	20	33 hours
24	75	2	47	1	15	20	39 hours
25	60	1	54	1	12	16	40 hours
26	58	1	65	2	15	17	38 hours
27	42	1	65	2	12	15	35 hours
28	34	1	73	1	14	15	38 hours
29	54	2	56	2	13	15	35 hours
30	42	1	65	1	15	18	39 hours
31	35	1	70	2	12	16	37 hours
32	26	1	56	2	16	18	38 hours
33	68	1	47	1	15	17	40 hours
34	56	2	54	2	16	18	37 hours
35	22	1	45	1	16	17	36 hours
36	16	1	56	2	16	17	36 hours
37	59	2	47	1	14	17	37 hours
38	49	1	65	2	16	18	35 hours
39	49	2	56	1	15	16	38 hours
40	39	1	56	1	16	18	40 hours
41	45	2	60	2	17	19	35 hours
42	22	1	65	2	16	18	35 hours
43	19	1	50	1	17	20	37 hours
44	61	2	49	2	16	19	34 hours
45	39	1	60	1	16	17	37 hours
46	43	1	74	2	16	20	35 hours
47	22	1	58	1	12	15	39 hours

48	56	2	65	1	15	17	38 hours
49	60	1	57	2	18	19	37 hours
50	18	1	60	2	17	20	35 hours
51	39	1	47	1	16	18	39 hours
52	58	2	56	1	18	20	41 hours
53	78	2	55	2	17	19	39 hours
54	16	1	64	1	15	18	39 hours
55	26	2	57	2	16	18	36 hours
56	46	1	67	1	15	17	38 hours
57	50	2	56	1	19	20	39 hours
58	51	2	58	2	17	19	36 hours
59	29	1	70	2	16	18	39 hours
60	24	2	64	1	15	17	36 hours